DISEASES OF THE THYROID GLAND

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BY

SAMUEL L GARGILL M D

Assistant Clinical Professor of Medicine Harvard Medical School, Visiting Physician Consultant to Endocrine Clinic and Head of the Fertility Clinic, Beth Israel Hospital Boston Mass

AND

MARK FALCON LESSES M D

Instructor in Medicine Harvard Medical School Visiting Physician, Chief of Endocrine Clinic and Director of Blood Bank, Beth Israel Hospital, Boston Mass

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THIS BOOK IS DEDICATED
IN GRATITUDE TO OUR RESPECTIVE WIVES
EILEEN R. CARGILL AND HELEN R. LESSES
FOR THEIR CO-OPERATION AND PATIENCE
WHILE THESE PAGES WERE BEING WRITTEN

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FOREWORD

Doctors Gargill and Lesses have given us a comprehensive, meticulous, and well arranged text on the thyroid They are well qualified to do this task having had many years experience in the field in the thyroid clinic of the Beth Israel Hospital Boston I have on several occasions visited this clinic and recognize its high standards of practice and study

The authors have covered the several diseases involving the thyroid gland thoroughly and they have prefaced their remarks with a full account of the underlying physiology

J H MEANS

PREFACE

Although there has been a spate of monographs and volumes dealing with the thyroid gland we were impelled to add another because of the need for a resynthesis of clinical and biochemical approaches to the diagnosis and treatment of thyroid disease The first twenty five years of clinical experience in the Endocrine Clinic of the Beth Israel Hospital afforded the basis for this presentation In point of time this quarter of a century overlaps three important eras in thyroid disease namely the utilization of stable iodine the use of anti thyroidal goitrogens and the application of radioactive iodine to the investigation and treatment of the normal and disturbed thyroid gland

We have attempted to cover thoroughly thyroid disease as we have seen it and know it in consequence some of the rarely encountered entities are omitted but this is counterbalanced by an extensive discussion of all of the commonly seen disturbances Newer aspects of the biochemistry and physiology of the thyroid are reviewed the interrelations of the thyroid with other endocrine glands are discussed at length the current place of the antithyroidal goitrogens in the treatment of thyrotoxicosis is elaborated the metabolism of iodine and its relation to the structure and function of the thyroid have been described so that

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the essential role of iodine in thyroid metabolism may be understood all the usual and some less usual clinical syndromes are presented and finally the insight into physiological and clinical phenomena afforded by radioactive iodine is repeatedly utilized

We acknowledge with thanks the many authors who have permitted us to reproduce important figures charts and photographs from their original publications We appreciate also the encouragement of the late Dr Henry A Christian who was largely responsible for our undertaking the preparation of this monograph To Dr Herrman L Blumgart Physician in chief at the Beth Israel Hospital we owe much for his interest Dr Felix Fleischner Director of Roentgenology at the Beth Israel Hospital helped in the selection of appropriate roentgenograms used as illustrations Dr Leopold Reiner Associate Pathologist at the Beth Israel Hospital selected the pathological material for photomicrographs reproduced throughout the monograph

SAMUEL L GARGILL M D
MARK FALCON LESSES M D

Boston Massachusetts
November 1954

CHAPTER XV A

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By Samuel L. Gargill and Mark Falcon Lesses

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PART I

ANATOMY, BIOCHEMISTRY, AND PHYSIOLOGY OF THE THYROID

Anatomy

In man the thyroid gland originates during the third week of embryonic life as an invagination of the pharyngeal entoderm anterior to the tracheal invagination. In later life the site of its origin is the foramen cecum located at the base of the tongue. At first a hollow tube, the thyroid anlage becomes a solid mass of cells which later descend through the thyroglossal tract into the anterior portion of the neck, forming epithelial bands and fenestrated plates. The primary thyroid follicles arise directly from these epithelial plates. The thyroglossal tract usually disappears early in embryonic life. Thus embryologically, the thyroid gland is a detached clump of entodermal tubules in front of the trachea.[1]

The human thyroid attains full size just before puberty. The gland normally comprises two lateral lobes connected by an isthmus. An additional lobe known as the pyramidal lobe may be present, especially in areas of endemic goiter. This lobe arises from epithelial rests along the thyroglossal tract and is recognizable as a strip of tissue reaching from the isthmus toward the hyoid bone on the left side of the thyroid cartilage. The adult thyroid normally weighs between 20 and 25 gm, averaging 0.4 gm per kilo of body weight; it is larger in women than in men. The whole gland is firmly attached to the trachea and therefore moves with that organ in swallowing.

The blood supply of the thyroid gland is of such magnitude that it clears the total blood volume of a normal man in about one hour. The blood is delivered to the gland through the four thyroid arteries, the right and left superior and inferior arteries. The superior descend from the external carotid artery to the upper poles of the thyroid. The inferior arise from the subclavian arteries to reach the posterior surface of the lower poles. Occasionally the median thyroidea ima artery is encountered ascending from the innominate artery in front of the trachea to

the lower portion of the thyroid gland These larger arteries divide and ramify over the surface of the gland whence penetrating vessels enter deeply into the thyroid structure forming a capillary bed around each follicle

The venous drainage starts from the perifollicular plexus and empties into the internal jugular veins by way of the superior and middle thyroid veins and into the innominate veins by way of the inferior thyroid veins Lymphatic drainage is provided by a perifollicular plexus which empties

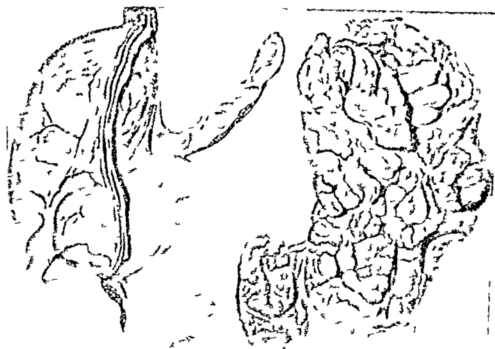


FIG 1 Normal human thyroid right and left lobes together with the isthmus The dotted line shows where the isthmus which in the section was left attached to the left lobe joins the base of the right lobe The right lobe is shown covered with fascia as it was found in the cadaver The anterior branch of the superior thyroid vessels is seen descending from the upper toward the lower pole From the junction of the upper portion of the right lobe can be seen a bizarre pyramidal lobe The isthmus and the left lobe are shown with all fibrous tissue investment including blood vessels nerves and lymphatics dissected away It is to be noted that there are no true lobules but a complex mass of parenchyma irregularly divided by an intricate anastomosing system of spaces or channels forming within the gland a veritable fenestrated labyrinth The gland as shown is made up of regions of connecting bars bands or plate like regions composed of individual discrete follicles or acini The stippled appearance of the surface represents the follicles From Rienhoff W F Jr Arch Surg 1929 xix 986 1036

into the deep cervical retrosternal tracheal and anterior laryngeal lymph nodes

Both sympathetic and parasympathetic fibers innervate the thyroid gland The sympathetic fibers are derived from the second to the fifth thoracic segments passing through the superior and middle cervical ganglia whence they are relayed to the gland through the superior laryngeal nerve and along blood vessels The parasympathetic fibers are derived from the vagus and enter the thyroid by way of the superior laryngeal nerve The exact role of the rich innervation of the thyroid is as yet undetermined it is clear that there is a complex and sensitive vasomotor control but it is uncertain whether nervous control of hormonal secretion exists



Fig 2 Cross section of normal human thyroid Cross section of the superior anterior region of the dissected left lobe shown in Fig 1 demonstrates anastomosing channels or spaces forming a fenestrated labyrinth It is to be noted that clefts do not completely *traverse the gland From Rienhoff W F Jr Arch Surg 1, 9 xix 98 1936*

The parenchyma of the thyroid has been shown by Rienhoff to be a complex mass of tissue irregularly subdivided into many areas These areas of tissue consist of groups of follicles of varying number size, and shape The parenchyma itself is unevenly compartmented by connective tissue septa which convey the blood vessels nerves and lymphatics (Figs 1 and 2)

The follicle is the structural and functional unit of the thyroid It is a cyst like structure varying in size from 50 to 1000 mu with an average measurement of about 300 mu A single layer of simple epithelial cells, low columnar or cuboidal, comprise the wall of the follicle within which there is a varying amount of a hyaline uniform material called *colloid* The follicles vary in shape from a sphere to a cube thus many are rounded while others are angular Each follicle is an isolated unit and evidence is lacking for any intercommunication (Fig 3)

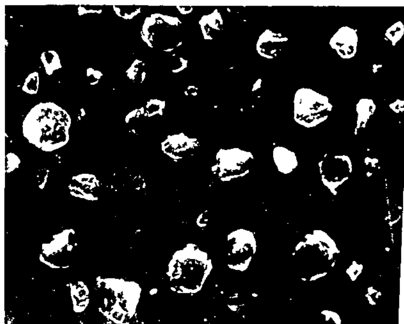


Fig 3 Group of follicles dissected from normal human thyroid Spherical shape together with the variability and thickness of the epithelial mass as evidenced by the difference in the photographic shadow cast is well brought out From Rienhoff W F Jr Arch Surg 19[illegible]9 xix 986 1036

The thyroid cell is a complex structure containing a large rounded reticular nucleus and cytoplasm in which special stains have demonstrated mitochondria and the Golgi apparatus The former are *granules or filaments* whose structure parallels quantitatively the secretory activity of the gland[3,4] The Golgi apparatus is a coarse thread like structure of the cytoplasm which occurs in the thyroid gland as well as in other secretory glands such as the pancreas and ovaries Its form and position vary with the activity of the cell and eventually it becomes fragmented

Cramer and Ludford[3] have advanced the interesting theory that the mitochondrial granules serve to increase or decrease the intracellular surfaces in accordance with secretory requirements Ingram[5] showed that the size of the Golgi apparatus is proportional to the size and secretory content of the follicular cells The height of the cell itself is a useful index of thyroid function for the cell elongates with increased activity and becomes flattened with rest[6]

The manner in which the thyroid cell secretes its hormonal produce has been demonstrated by Williams[7] who observed living thyroid follicles implanted in the ear of the rabbit The follicles underwent cyclic changes in activity divisible into these four stages (1) secretion characterized by an increasing refractility of the thickened walls and by the roundness of both follicle and colloid (2) secretion and colloid release characterized by further increase in refractility of the walls with diminution in their thickness increase in colloid and in active follicles by irregularity of the internal border of the wall the irregularity being explained tentatively as due partly to compression of exhausted cells to such a degree that diffusion of colloid across them can take place this appears to be the chief mechanism of colloid release (3) partial collapse caused by colloid release at greater velocity than colloid production (4) recuperation characterized by an opacity of the walls which are thickened and enclose very little colloid Williams concluded that secretion is toward and into the lumen by diffusion

The nervous innervation of the follicle appeared to play no part in secretion under the conditions of his experiment On the other hand anterior pituitary extracts containing the thyrotrophic hormone augmented colloid production and release

The mechanism of release of follicular colloid in man has been considerably elucidated in studies on necturus by Grant[8] who demonstrated that stored colloid emptied into the blood capillaries surrounding the follicles under the influence of anterior pituitary implantation As a consequence of her experiments she has advanced a theory of transcellular colloid release During the transfer stage the colloid in the follicle cells is seen first as large refractile droplets which later appear fine and emulsified Since the follicles showed progressive emptying the colloid content of the cells must be regarded as proof of transcellular colloid release rather than as a product of synthesis The mechanism by which the colloid crosses the cell boundary is unknown though emulsification enzymatic digestion and phagocytosis have been variously advanced as possible explanations In the mammalian gland the follicular cells per-

haps transport the colloid through their cytoplasm in an unstainable form in necturus one can obtain histological proof of this method of colloid export

Gersh and Caspersson [9] through studies of frozen dried thyroid gland sections with the ultraviolet microscope have contributed significantly to the understanding of colloid release Thyroglobulin has a characteristic absorption curve in the ultraviolet region of the spectrum with absorption characteristics allowing separation of tyrosine and tryptophane on the one hand and thyroxine and diiodotyrosine on the other Application of this knowledge through methods developed by Caspersson allowed the quantitative concentration of total protein in the colloid and of thyroxine and diiodotyrosine in both colloid and cells to be determined The protein bound iodine comprising thyroxine and diiodotyrosine was found homogeneously distributed in the colloid The administration of potassium iodide or anterior pituitary extract produced continual secretion of colloid into the lumen for storage and subsequent reabsorption Markedly stimulated glands showed secretion directly toward the blood vessels

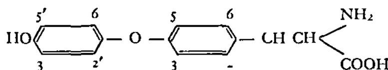
Dempsey [10] has also investigated the histochemistry of the thyroid through a study of its fluorescent qualities Intrafollicular colloid the follicular cells connective tissue and thyroid pigment revealed autofluorescence when viewed through an ordinary microscope illuminated with ultraviolet rays Deficient fluorescence of the colloid occurred in iodine and hormone deficient glands Further studies of the chemical cytology of the thyroid by Dempsey and Singer [11] have provided evidence that the colloid contains a conjugated protein ribonucleoprotein in addition to the simple protein thyroglobulin The significance of this finding in relation to thyroid physiology is at present unclear These authors and others have found both alkaline and acid phosphatases in the thyroid gland apparently participating in its intermediary carbohydrate metabolism The phosphatases are deposited in varying concentration in some of the endothelial cells of the capillaries thus suggesting a mechanism for controlling migration of metabolites through the capillary wall (Plates 1 and 2)

BIOCHEMISTRY

The epithelial cells of the follicle secrete the colloid substance which is stored within the lumen The thyroid hormone is ordinarily contained

in this material and thus it represents a unique example of an internal secretion that can be visualized with the microscope. Thyroglobulin can be extracted from the gland with physiological salt solution and by appropriate precipitation with varying concentrations of ammonium sulfate its proteins may be salted out.[1] Bauman[13] in 1896 first showed that the thyroid protein contained iodine and that the iodine in the gland was organically bound. Hutchison[14, 15] recognized that the protein was globulin and later investigation has demonstrated that except for its iodine content this iodo-thyroglobulin does not differ markedly from other globulins of animal origin.[16] The molecular weight of thyroglobulin has been determined to be about 675 000.[17]

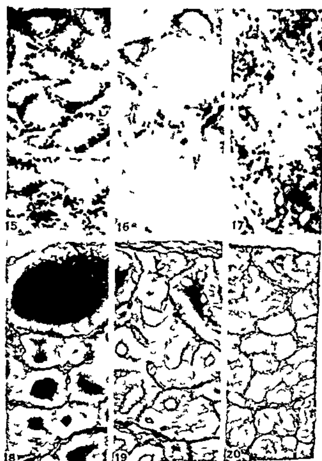
The iodine of the thyroid is derived immediately from the circulating blood and ultimately from the iodides and iodates of ingested food and water. Iodates are converted to iodides in the intestinal tract and are absorbed in the latter form. By means of radioactive iodine[18] it has been established that the thyroid of the normal rabbit is saturated with the halogen within 15 minutes after an intravenous iodine injection. The iodine thus acquired is organically bound for hormone synthesis or rediffuses into the blood stream. The normal thyroid gland does, however, contain 7 per cent of its total iodine in inorganic form.



DL-THYRONINE

The physiological potency of thyroglobulin depends chiefly upon its content of two iodine-containing amino acids, namely, thyroxine and diiodotyrosine, the former probably accounting for 9 per cent and the latter for 64 per cent of the total iodine in the normal gland. Thyroxine containing 65 per cent iodine was isolated by Kendall in 1915.[19] Harington[0] proved that thyroxine is an amino acid with four iodine atoms, a hydroxyphenyl ether of tyrosine or 3, 5, 3, 5 tetra-iodothyronine. Harington and Barger[1] later synthesized thyroxine by conjugating two molecules of diiodotyrosine.

Plate 1



15 Fructose diphosphatase reaction pH 9.5 in the endothelial and follicular cells of the thyroid gland from a normal control rat. The section was incubated for 4 hours in the substrate mixture and the precipitated phosphate was visualized by transformation to cobaltous sulfide. Fixation in cold 80 per cent alcohol.

16 Thyroid gland from a rat exposed to cold illustrating the reduction in the alkaline fructose diphosphatase reaction. The enzyme does not appear in the endothelium or parenchymal cells associated with the central or most active follicles, but is restricted to the peripheral inactive portions of the gland. Fixation in cold 80 per cent alcohol.

17 Alkaline fructose diphosphatase in the thyroid gland of a rat to which thiouracil had been administered. Fixation in cold 80 per cent alcohol.

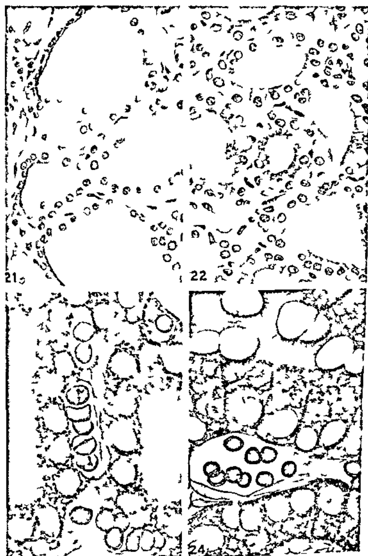
18 Argyrophilia of the colloid from the thyroid gland of a normal control rat. Bouin fixation section digested in saliva. Pap's stain.

19 Section illustrating the reduction in argyrophilia particularly in the central follicles from a rat exposed to cold. Bouin fixation section digested in saliva. Pap's stain.

20 Section illustrating the further reduction in argyrophilia in the thyroid gland of a rat to which thiouracil had been administered. Bouin fixation. Sections digested in saliva. Pap's stain.

From Dempsey, E. W. and Singer, M. Endocrinology 1946 xxxviii 270-95

Plate 2



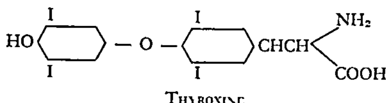
21 Drawing illustrating the localization of alkaline glycerophosphatase (pH 9.4) in the follicular cells of peripheral follicles from the thyroid gland of a normal control rat The endothelial cells are negative Fixation in cold 80 per cent alcohol Section incubated in substrate mixture for 6 hours

22 Drawing illustrating the localization of acid glycerophosphatase in the nuclei and parenchymal cells of the central follicles from the thyroid gland of a rat exposed to cold Fixation in 80 per cent alcohol Section incubated 48 hours

23 Drawing illustrating the argyophilic granules of the follicular epithelium of a normal control rat This appearance has been observed only after Zenker fixation

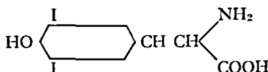
24 Argyrophilic granules in the thyroid gland from a rat after exposure to cold Zenker Fixation Pap's stain

From Dempsey W W and Singer M Endocrinology 1946 xxxviii 270–95



THYROXINE

This compound has been isolated in pure form from the gland by Oswald in 1911 and from the colloid by Harington and Randall in 19 9[3] Diiodotyrosine has the following structural formula



The biosynthesis of thyroxine appears to involve two stages first the iodination of tyrosine second the coupling of two molecules of diiodo tyrosine to form thyroxine The derivation of diiodotyrosine from the essential amino acid tyrosine has been established by various methods It probably involves oxidative processes capable of liberating iodine from iodide to make it available for attachment to the tyrosine molecule Cavett[4] analyzed various thyroglobulins with regard to their amino acid content and found the tyrosine content to vary inversely with the content of thyroxine and diiodotyrosine He also showed that thyroglobulins low in iodine had a greater content of tyrosine and conversely that thyroglobulin from the glands of patients treated with iodine had more diiodotyrosine and thyroxine and less tyrosine This ability of the thyroglobulin molecule to alter its composition of amino acids explains the mechanism whereby iodine content and physiological potency of thyroglobulin may be varied

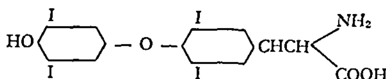
Further proof that iodination of tyrosine is the first step in the synthesis of thyroxine has been furnished through the use of radioactive iodine as a tracer substance This has been utilized by injecting radio iodine into animals and determining the subsequent distribution of radio activity in the body or by studying the respiration of thyroid tissue slices in a medium to which radioactive iodine had been added and whose fate could be traced Following the injection of radio-iodine into animals there is rapid concentration of iodine in the thyroid gland [3 7] This occurs quickly within a matter of minutes and proceeds until as

much as 50 per cent of the radioactive material is found in the thyroid gland after 48 hours With tracer doses Morton and his co workers have repeatedly shown that almost all of the radio iodine deposited in the gland is organically bound within one hour The radioactive iodine is distributed among three fractions inorganic iodide diiodotyrosine and thyroxine With passage of time there is gradual increase in the amounts of diiodotyrosine and thyroxine and decreasing amounts of inorganic iodide This work combined with the studies of Cavett mentioned above shows clearly the reciprocal relationship existing among tyrosine inorganic iodide diiodotyrosine and thyroxine

When large amounts of radioactive iodine are added to the medium in which surviving thyroid tissue slices are respiring there is rapid incorporation of the radio iodine in the tissue As in the *in vivo* experiments the radioactivity is associated at first with diiodotyrosine and later appears with thyroxine thus indicating a process of conversion similar to that seen in the intact animal [3] It is of interest however that Schachner Franklin and Chaikoff [31] demonstrated that surviving thyroid slices were able to concentrate up to 60 per cent of added radio iodine even after the inhibition of thyroxine and diiodotyrosine formation by azide or sulfanilamide Cyanide and sulfide in addition to inhibiting thyroxine and diiodotyrosine formation also blocked the accumulation of radio iodine by thyroid slices From this selective blocking of iodine concentration and thyroxine formation these authors concluded that thyroid tissue possesses an additional mechanism for concentrating iodine that does not depend upon conversion of inorganic iodide to thyroxine and diiodotyrosine

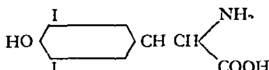
The role of tyrosine in the synthesis of thyroxine and as a scaffold for the attachment of iodine to the protein molecule may be best appreciated by Harington s statement [3] that it is possible by choosing the proper conditions almost to titrate the tyrosine in a protein with iodine While thyroxine and diiodotyrosine are the major iodine-containing compounds of the thyroid chromatography has demonstrated that others are present particularly monoiodotyrosine [4, 38] in amounts up to 15 per cent of the total iodine

Iodination of tyrosine is the first step in hormone synthesis The coupling of diiodotyrosine to form thyroxine as the final step in the process must be considered in relation to certain enzyme systems that are involved in intracellular respiration Oxidation within the cell requires enzymatic action because the usual metabolites of the body are not auto oxidizable There are cellular iron containing pigments known as cyto



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cytochrome C cytochrome oxidase system using an enzyme preparation from the rat heart

Thyroglobulin thus appears as a complex protein which incorporates three iodine containing amino acids in its molecule through iodination of tyrosine The iodine content of the normal human thyroid varies from 0 05 to 0 45 per cent of the dry gland[43] or from 0 to 4 5 mg per gram of dried thyroid The average iodine content of dried glands throughout the world is close to 0 per cent[44] (mg per gram dried gland) The iodine content varies depending upon the activity of the gland season of the year geography and food habits[43, 45, 47]

While the thyroid gland selectively fixes about 0 per cent of the body s iodine organically bound iodine is present in other tissues and thyroxine like fractions have been biologically demonstrated in these tissues The role of this extrathyroidal organic iodine is not clear but is undoubtedly significant

Chapman[46] found that the level of iodine intake had a pronounced effect on the weight surface area metabolic rate and food utilization of thyroidectomized animals those with higher iodine ingestion showing an effect which suggested that iodine might play a role in production of a thyroxine like substance in the tissues This aspect of extrathyroidal hormone production was more definitely established by Morton Chaikoff and their collaborators[49] through the use of radioactive iodine From to 8 months following thyroidectomy radio iodine was injected into young rats who were then killed at intervals of to 96 hours after the injection Measurable quantities of labeled thyroxine and diiodotyrosine were found in the liver muscles and small intestines The completeness of the thyroidectomy was checked both by serial section and by the radio autographic technique

These experiments indicate that tissues other than the thyroid possess the ability to elaborate small amounts of a thyroid like substance Harington[2] explains the extrathyroidal synthesis of thyroxine as a general biological function of almost any living tissue containing adequate amounts of iodide since tissue proteins will contain tyrosine bound in a peptide linkage whence it can undergo the reactions leading to thyroxine This would leave the thyroid gland the specific functions of concentrating iodine in large amounts of increasing the rate of formation of thyroxine and of storage of iodine containing amino acids in the form of thyroglobulin The possibility of this extrathyroidal synthesis of thyroxine is not surprising in view of studies on artificial iodo proteins Oswald isolated crystalline diiodotyrosine from hydrolysates of iodi

chrome a b and c which are widely distributed in aerobic cells of many kinds and are especially abundant in tissues with large oxygen consumption Oxidation of these pigments by molecular oxygen is accomplished by a respiratory enzyme known as cytochrome oxidase This enzyme which is readily inhibited by cyanide is especially important in the oxidation of cytochrome a and c less so for b which is to some extent self oxidizing [3] With the aid of radio iodine Schachner Franklin and Chaikoff [36] have demonstrated that the formation of both diiodotyrosine and thyroxine in the thyroid is accomplished through intracellular aerobic oxidations involving the cytochrome oxidase system The need for cellular organization was indicated by the fact that homogenized thyroid tissue had lost its capacity to incorporate radio iodine This incorporation does not occur with complete anerobiosis Furthermore typical inhibitors of cytochrome oxidase such as cyanide, azide sulfide or carbon monoxide block the formation of diiodotyrosine and thyroxine from inorganic iodide in thyroid slices Dempsey [10] has found cytochrome oxidase in the cells of the thyroid follicle and has also presented evidence for the presence of peroxidase in the thyroid cells The peroxidase reaction was easily inhibited by thiouracil whereas the cytochrome-oxidase reaction was unaffected DeRobertis and Grasso [37] have confirmed these findings

Harington [38, 39] has postulated that the enzymic oxidizing system liberates iodine from iodides and that this free iodine is the effective oxidizing agent which converts both tyrosine to monoiodotyrosine and diiodotyrosine and the latter to thyroxine According to Harington [39] diiodotyrosine or its derivatives in alkaline solution speedily liberate small amounts of iodine so that it is readily available as an oxidizing agent Mild reducing agents that react with iodine such as thiosulfate and many antithyroid drugs inhibit this reaction Further support to this view has been lent by Keston [40] who found that iodine and oxidases participate in the reaction which organically binds iodine Recently Reineke and Turner [41] after a study of the factors influencing the iodination of casein concluded that manganese had an important catalytic role in the promotion in vivo of thyroxine formation Ray and Deysach [42] had earlier shown the particular ability of the thyroid to store manganese

Thyroxine itself has an important role in enzymatic mechanisms Gemmill [43] demonstrated that thyroxine increases the rate of oxidation of the ascorbic acid-ascorbic acid oxidase system (plant origin) and inhibits the cupric ion catalyzed oxidation of ascorbic acid Thyroxine was also found to stimulate the oxidation of succinate in the dehydrogenase-

cytochrome C cytochrome oxidase system using an enzyme preparation from the rat heart

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Chapman [48] found that the level of iodine intake had a pronounced effect on the weight surface area metabolic rate and food utilization of thyroidectomized animals those with higher iodine ingestion showing an effect which suggested that iodine might play a role in production of a thyroxine like substance in the tissues This aspect of extrathyroidal hormone production was more definitely established by Morton Chai koff and their collaborators [49] through the use of radioactive iodine From - to 8 months following thyroidectomy radio iodine was injected into young rats who were then killed at intervals of - to 96 hours after the injection Measurable quantities of labeled thyroxine and diiodotyro sine were found in the liver muscles and small intestines The complete ness of the thyroidectomy was checked both by serial section and by the radio autographic technique

These experiments indicate that tissues other than the thyroid possess the ability to elaborate small amounts of a thyroid like substance Harington explains the extrathyroidal synthesis of thyroxine as a general biological function of almost any living tissue containing ade quate amounts of iodide since tissue proteins will contain tyrosine bound in a peptide linkage whence it can undergo the reactions leading to thy roxine This would leave the thyroid gland the specific functions of con centrating iodine in large amounts of increasing the rate of formation of thyroxine and of storage of iodine containing amino acids in the form of thyroglobulin The possibility of this extrathyroidal synthesis of thy roxine is not surprising in view of studies on artificial iodo proteins Oswald isolated crystalline diiodotyrosine from hydrolysates of iodi

nated albumin casein and gliadin Ludwig and von Mutzenbecher[50] iodinated casein and other proteins thus producing products whose physiological activity was shown to be due to contained thyroxine and from which thyroxine was actually isolated Harington and Pitt-Rivers have confirmed this work[51] These artificial iodo-proteins and various fractions of their hydrolysates have physiological effects similar to those of the thyroid hormone [53] The iodinated proteins are of more than theoretical interest as a source of thyroxine containing protein Reineke and Turner[54] have successfully produced synthetic thyro proteins which have several times the thyroidal activity of U S P thyroid powder, as judged by assay on tadpoles or by yield of thyroxine This increased activity appears entirely explicable on the basis of a content of thyroxine more than three times that normally obtained in powders derived from the dried gland Of considerable interest in connection with this finding is the further fact that the iodination of protein yields maximal thyroidal activity with substitution of two atoms of iodine per molecule of tyrosine An increase in iodination beyond this yields products of lesser activity Co-operative studies [55] in England have shown that iodinated casein as well as other iodinated proteins serve as an adequate stimulant of milk yield in the cow in a manner exactly similar to dried thyroid gland and thyroxine Such proteins also maintain growth in young thyroidectomized rats and effect premature metamorphosis in tadpoles

Only two mechanisms are available to explain the formation of thyroxine which has been proved to follow the iodination of proteins (1) either the protein contained thyronine (this is thyroxine less all four of its iodine atoms) which directly added iodine to form thyroxine, or (2) the iodine produced diiodotyrosine from tyrosine and was then converted into thyroxine The latter process is perhaps the more likely and has been demonstrated by von Mutzenbecher to occur in minimal amounts as mentioned previously Thus the synthesis of thyroid hormone in the body and the iodination of protein in the test tube appear to follow a similar chemical pattern

The chemical structure of thyroxine has been shown to be specific by Harington and McCartney [56] who found a chemical isomer of thyroxine lacking the thyronine configuration to be inert This has been confirmed and extended by other workers who have shown that a high specificity of structure is required to produce significant activity Substitution of the iodine atoms in unusual places (e g at positions 4′ 6) strikingly reduced activity [57] Niemann[58] has exhaustively reviewed the chemistry of thyroxine and related compounds

Harington has demonstrated that naturally occurring thyroxine is 3,5,3',5'-tetraiodo-L-thyronine. The non-halogenated amino acid DL-thyronine, which resembles thyroxine structurally, lacks thyroxine-like activity. The addition of iodine in the 3 and 5 positions to thyronine produces some thyromimetic action at a level of 1/15 to 1/40 of that of DL-thyroxine. If other halogens, namely chlorine, bromine and fluorine, are added to thyronine, thyroxine-like activity develops, but none is so potent as iodine. Harington has concluded that thyromimetic activity develops only when the halogen atoms are present in the 3 and 5 positions of the thyronine nucleus. Lerman, Harington and Means[24] have found that the substitution of bromine or chlorine for iodine diminishes considerably the activity of the thyroxine molecule. Tetrabromthyronine has 3 per cent and tetrachlorthyronine has 0.5 per cent of the activity of L-thyroxine.

Naturally occurring thyroxine is levorotatory. Commercially available thyroxine has usually been racemic (that is, DL-thyroxine) because it has been easier to isolate and synthesize in this form. L-thyroxine, however, is now commercially available and has been found by us to be effective in the treatment of myxedema. The L-isomer is much more potent than D-thyroxine, according to Gaddum.[2] Reineke and Turner[60] consider the activity of DL-thyroxine to be due entirely to the presence of the L-isomer.

These biological mechanisms for incorporating iodine into the body chemistry present the unsolved question of why the organism has selected iodine from among the elements to aid in the formation of an important cellular stimulant. The intimate relation of iodine to the sea suggests an ancient paleochemical origin of the hormone. Chlorine, another halogen, had already been utilized to form an essential component of the marine environment of our ancestors as well as an abundant component of human blood. The question cannot, of course, be answered but serves to focus attention on the chemical genealogy of the hormone.

The Nature of the Circulating Hormone

While the nature of the circulating hormone is at present unclear, it is established that it lies somewhere between the large moleculed protein thyroglobulin and the relatively simple iodine-containing amino acid thyroxine, if in fact it is not either thyroglobulin or thyroxine. Thyroglobulin, which appears to be the form in which the hormone is present

in the gland itself has not been found as such in the circulating blood except in the thyroid veins during or immediately after thyroidectomy for toxic goiter Since Hektoen and his co workers[61 62] demonstrated that highly sensitive precipitin reactions to thyroglobulin could be developed through the use of immune serum the problem has been approached immunologically This earlier work was extended by Lerman[63] who was unable to demonstrate thyroglobulin in the serum of thyrotoxic or normal persons More direct evidence excluding thyroglobulin itself as the circulating hormone has been offered by Bassett Coons and Salter,[64] who found the major part of the circulating iodine in the albumin fraction albeit the highest concentration of iodine was in the alpha and beta globulins

Harington[65] has presented immunological experiments which support his view that thyroxine is the effective form of the circulating hormone He immunized animals with artificial thyroxine protein complexes whose antigenic specificity was determined by thyroxine and diiodotyrosine groups The antibodies of the antiserum thus produced were specifically adapted to combine with the molecule of the physiologically active substance and thus were able to interfere with the action of this substance in another animal by a process analogous with passive immunization The antisera thus developed against the thyroxine-protein complexes did not lower the metabolic rate of normal animals but did prevent the characteristic rise in metabolic rate caused by thyroglobulin or thyroxine This neutralization of the effect of thyroxine by the antisera showed that the circulating antibodies containing combining sites adapted to thyroxine interfered with the access of the latter to its normal sites of action in the tissues

Harington s hypothesis is only weakened by the work of Canzanelli and Rapport[66 67] who found significant metabolic effects produced by thyroglobulin upon tissues in vitro and an absence of such effects by thyroxine Barker[68] as well as Williams-Ashman[69] however have found no in vitro effectiveness of thyroglobulin

Craig and Salter[70] found that thyroxine when added to normal blood did not induce the calorigenic action in excised surviving tissues that was readily produced by the blood of thyroxinized animals thus suggesting that thyroxine is altered in some way before becoming the effective form of the hormone Thyroxine however has been found a complete metabolic substitute for the functioning thyroid gland in the living organism

Gross and his associates[70] found that thyroxine after its release by the thyroid gland circulates in combination with plasma proteins This

combination may be readily separated by butanol but is reconstituted when thyroxine is placed in contact with plasma proteins. In further attempts to identify iodine compounds other than thyroxine and iodide in human plasma, Gross and Pitt-Rivers [illegible] succeeded in demonstrating the presence of an iodine-containing substance in the plasma of patients given radioactive iodine which behaved in a manner identical with that of 3:5:3'-triiodothyronine on two-dimensional paper chromatograms and on a kieselguhr column. They concluded that this substance, triiodothyronine, is a normal constituent of the organic iodide fraction of plasma since they found it in the plasmas of both euthyroid and hyperthyroid individuals. The steps in the biological synthesis of thyroid hormone they formulated as follows: (1) oxidation of iodide to iodine, (2) iodination of tyrosine to diiodotyrosine, (3) coupling of 2 molecules of diiodotyrosine to give 1 molecule of thyroxine, and (4) deiodination of thyroxine to give triiodothyronine.

Triiodothyronine was then assayed in thiouracil-treated rats by its effect in preventing goiter.[78] The activity of triiodothyronine was found to be about three times that of L-thyroxine, and it was concluded that triiodothyronine is probably the form of the thyroid hormone that is active in the tissues. Its effect in myxedema was then studied[79] by administering it to two hypothyroid patients in a daily dose of 80 micrograms. This dose had an effect similar to that of a daily oral dose of 100 to 300 micrograms of L-thyroxine; the basal metabolic rate and blood cholesterol levels returned to normal and at the same time the patients lost weight during the treatment.

The metabolic effects of triiodothyronine as well as the metabolism and distribution of radioactive triiodothyronine have been further studied. Asper and his co-workers[9] observed that triiodothyronine produced an immediate metabolic effect five to ten times that of equivalent doses of L-thyroxine in patients with myxedema. Within six hours after its administration in a single subcutaneous dose (0.5 to 1.0 mg.), progressive increases in pulse rate and body temperature occurred, reaching a maximum on the third day. The basal metabolic rate increased promptly and there was acceleration of urinary creatine excretion as well as nitrogen and phosphorus diuresis with resultant negative nitrogen and phosphorus balances and weight loss. The serum protein-bound iodine levels increased after administration of triiodothyronine although they frequently remained in the hypothyroid range when the patients were metabolically euthyroid. L-thyroxine, on the other hand, increased the PBI values to euthyroid levels although the

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the enterohepatic circulation Both substances rapidly disappeared from the body after 15 days 1 5 per cent of triiodothyronine and 5 per cent of thyroxine radioactivity remained After injection of triiodothyronine 54 8 per cent of excreted I^{131} appeared in the urine compared with 36 per cent after injection of thyroxine Thyroxine was selectively retained in the liver so that after 15 days more than 55 per cent of residual radioactivity was in the liver and less than 40 per cent in the carcass Fifteen days after triiodothyronine injection virtually all radio activity was either in the thyroid or in the carcass This again suggests that triiodothyronine may be the active form of the hormone in the tissues

If the circulating hormone is thyroxine or some other hydrolytic product of thyroglobulin there should exist an enzyme system in the gland itself capable of breaking down thyroglobulin by proteolysis into smaller components which can cross cell membranes The existence of such an enzyme system has been demonstrated and its activities quantitated by DeRobertis and Nowinski [1] who measured proteolytic activity by determining the formation of tyrosine and tryptophane from the protein edestin through the action of excised human thyroid glands They found approximately a 100 per cent increase in proteolytic activity in the thyrotoxic gland as compared with the normal and about a 5 per cent decrease in iodized thyrotoxic glands and in non toxic diffuse goiters

Physiology

If thyroglobulin is essentially the storage form of the thyroid hormone then one would expect thyroxine to be the amino acid to which it owes all of its activity The results of physiological assays have proved contradictory however While thyroxine completely relieves human myxedema it has been claimed that desiccated thyroid or thyroglobulin produces a calorigenic effect greater than can be accounted for by their thyroxine content Thus Reid Hunt showed by means of the acetonitril test that desiccated thyroid produced an effect greater than the equivalent amount of thyroxine (as iodine) in protecting mice against cyanide poisoning This presumed superior effectiveness of thyroglobulin and desiccated thyroid cannot be due to a simple summation of the activity of diiodotyrosine and thyroxine because the former by itself has but little calorigenic effect [73,74] Moreover 3 5 diiodothyronine (thyroxine less two of its iodine atoms) has but 4 per cent of the activity

patients were still hypothyroid Serum cholesterol levels decreased following the administration of either compound but the decrement bore no quantitative relationship to the degree of metabolic change Electrocardiograms reverted more rapidly to normal after triiodothyronine than after L thyroxine therapy

The paradoxical effect of triiodothyronine on the serum protein bound iodine was also noted by Starr and Liebhold Schneck[70g] who found that sodium levothyroxine in a dosage of 0.075 mg orally usually reduced radioactive iodine uptake by the thyroid of normal human subjects and that this was associated with a rise of protein bound iodine *when a dosage of 0.[illegible] mg or more was given whereas triiodothyronine* in a dosage as low as 0.008 mg orally also reduced the uptake but was associated with a decrease in serum protein bound iodine

Blackburn and his associates[71] compared the calorigenic effects of triiodothyronine and thyroxine given intravenously to myxedematous patients The initial response to triiodothyronine appeared sooner and reached a maximum in 24 to 48 hours whereas the maximal response to thyroxine occurred in 7 to 10 days The biologic decay rate of the two substances was found to be similar and possibly identical and therefore Blackburn and his co-workers concluded that the total calorigenic effects were substantially the same Wiswell and Asper[70] found that triiodothyronine like thyroxine was not effective in stimulating oxygen consumption when added directly to intact tissues incubated in vitro but was more potent than thyroxine in accelerating the oxygen utilization of tissues from animals injected with these compounds and of a specific rat-heart homogenate system to which these substances have been added

Rall and his co workers[70i] studied the metabolism of radioactive triiodothyronine L-thyroxine and D-thyroxine in subjects with and without thyroids and in one individual with a complete biliary fistula They found that the optical isomers of thyroxine were metabolized at markedly different rates although they were distributed in a similar manner in the body fluids whereas triiodothyronine was metabolized at a much faster rate than L-thyroxine and although initially it was distributed in a space similar to that of thyroxine the final value of distribution exceeded the body weight Keating and Albert[k] compared the distribution and metabolism of radioactive triiodothyronine with that of radioactive L thyroxine by injecting physiological doses of either compound into immature rats Both substances were distributed immediately and identically in the liver and were similarly massive in

decay to range from 0 to 0 4 mg of thyroxine daily indicating that the same amount would be required to maintain a normal basal metabolic rate in a patient with complete myxedema Thompson and his co-workers[a] later found that 0 3 to 0 4 mg daily of thyroxine was in fact the necessary maintenance dosage in such patients

The duration of action representing the total period of incubation activity and decay varies to some extent in accordance with the method of measurement the manner of administration and the form and amount of the hormone utilized Thus Gaddum[83] found thyroxine to be effective for 3 days when given intravenously and for 3 weeks when administered subcutaneously Salter Lerman and Means[84] found thyroxine polypeptide to be effective for 90 days whether given orally or intravenously Thompson[85] found intravenous thyroxine active over a period of 90 days and desiccated thyroid over a period of 69 days Hughes[86] has measured the duration of action of single doses of thyroxine and desiccated thyroid in rats pre treated with thiouracil This drug prevents synthesis of thyroid hormone and results in compensatory hyperplasia and lowered iodine content of the thyroid Administration of thyroxine or desiccated thyroid will prevent these effects and therefore the duration of their actions may be measured by ascertaining the onset of hyperplasia through the determination of increased gland weight Hughes observed much shorter duration of action even with large doses than the majority of previous investigators Small doses lasted 3 to 1 days and large doses given intra peritoneally were completely metabolized within one month Subcutaneous or intravenous injections of thyroxine were effective for as long as thyroid powder by mouth He believes this method is more accurate in measuring duration of action of thyroid hormone than the basal metabolic rate Reineke and his co workers[87] have also found this technique comparable with the standard metabolic method of performing thyroid assays or measurements of thyroid function (Figs 4 and 5)

The metabolism of thyroxine has been more carefully studied since 1944 when Joliot and his associates first described the preparation of radioactive thyroxine and its behavior in the organism[7] [8] Albert and his co-workers[8] [8,8,87] have investigated the role of the gastro intestinal tract and the liver in the metabolism of radiothyroxine by the intravenous injection of physiological doses of radioactive 1 thyroxine into immature male rats They observed an immediate distribution of the injected material in the blood (38 per cent of the dose) the liver (30 per cent) and the remaining tissues of the body (3- per cent) After this initial

of thyroxine The organic iodine content of the whole thyroid gland is due almost entirely to thyroxine and diiodotyrosine The calorigenic action has been claimed by Means and his associates [6] to depend upon this total organic iodine rather than upon thyroxine content alone On the other hand, Palmer and Leland [7] concluded that thyroxine alone determined the calorigenic effect of thyroid and they were able satisfactorily to explain the apparent correlation between total organic iodine of the thyroid and calorigenic activity reported by Hunt and Krogh and Lindberg [8] as due to a fortuitous parallelism between total and thyroxine iodine content Subsequently McClendon Foster and Cavett [79] after studying the calorigenic action of thyroglobulins with varying thyroxine content upon the metabolic rate of rats concluded that the calorigenic effect of thyroglobulin depended on its thyroxine content alone Harington [6] also expresses doubt concerning the adequacy of the evidence relating the activity of the thyroid gland to its total iodine content rather than to its thyroxine iodine content

Two aspects of thyroid physiology common to all its actions are the phenomena of latency of activation and decay These manifestations are apparent either following the administration of the hormone to the thyroid less individual or following removal or atrophy of the gland When thyroxine is administered intravenously to the hypothyroid subject no discernible effect is seen until about 12 hours have elapsed [80] Following this period there develops an increased rate of metabolism which reaches a maximum on the fourth day and then gradually declines over a period of 4 to 6 weeks to the initial level The curve of activation and inactivation or decay following a given dose of thyroxine or dried thyroid gland follows a definite pattern which may be expressed mathematically with some accuracy Briefly these curves are exponential rather than arithmetic and indicate that crystalline thyroxine must be activated before it can function The phases of activity of thyroxine in dried thyroid may therefore be divided into these three according to Boothby (1) the period of incubation (2) the period of increased activity and (3) the period of decay

When the thyroid gland is removed or undergoes spontaneous atrophy progressive inactivation or decay of the hormone takes place The same phenomena may be observed when thyroid medication is discontinued in a myxedematous patient who has received sufficient thyroid to maintain a standard metabolic rate The rate of inactivation is exponential and follows a gently sloping curve which takes 70 to 80 days for completion Plummer and Boothby [81] found the daily rate of thyroxine

1 per cent per hour More than one half of the residual radioactivity was in the liver 16 days following injection

The proportion of endogenously I^{131} labeled thyroid hormone in the thyroid carcass gastro intestinal tract and liver and the rates of movement of labeled hormone in these compartments and in the excreta

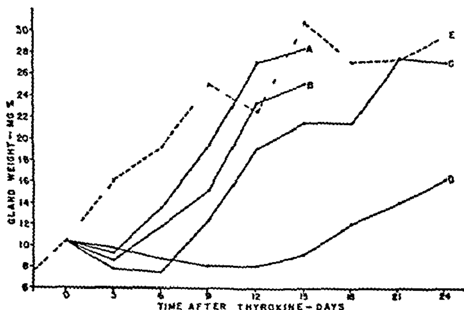


Fig 5 Effects of a single injection of thyroxin on the rate of enlargement of the thyroid glands of thiouracil treated rats A = 10 ug (solution) B = 100 ug (solution) C = 1 mg (solution) D = 1 mg (suspension) E = control animals receiving thiouracil alone The initial point indicates the gland weight at the beginning of thiouracil administration and o the time when thyroxin was injected Each point represents the average of 5 or more animals From Hugh A M Endocrinology 1945 xxxvii 280 85

were next determined under conditions of experimentally altered thyroid function in immature rats The thyroids of these rats were labeled with I^{131} and then exposed to agents or procedures that caused either liberation or retention of labeled hormone The proportions of I^{131} in the thyroid gastro intestinal tract and carcass were determined Thiouracil caused an intense loss of thyroidal I^{131} and a symmetrical increase in I^{131} of the gastro intestinal tract and carcass Thyrotrophin induced similar but less intense loss of thyroidal I^{131} and a symmetrical gain in I^{131} of the carcass and gastro intestinal tract Hypophysectomy or

distribution rapid diffusion occurred into the gastro intestinal tract chiefly by way of bile but probably also by direct secretion At equilibrium the gastro intestinal tract contained at any time about one half of the circulating radiothyroxine or intermediates thereof A massive recirculation of radioactivity occurred from the bowel presumably via the portal and lymphatic drainage The rapidity of the recirculation was

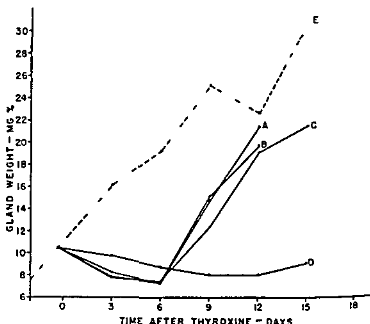


Fig 4 A comparison of the effect of single doses of thyroid hormone given by various routes to thiouracil treated rats A = 1 mg thyroxin in solution intravenously B = 500 mg desiccated thyroid by stomach tube C = 1 mg thyroxin in solution subcutaneously D = 1 mg thyroxin suspension subcutaneously E = control animals receiving thiouracil alone The initial point indicates the gland weight at the beginning of thiouracil treatment and 0 the time of thyroid hormone administration Each point represents the average of 5 or more animals From Hughs A M Endocrinology 1945 xxxvii 280 85

emphasized by the disparity between the rate at which radioactivity was secreted into the bowel more than 100 per cent per hour and the rate at which it left the bowel in the feces about 3 per cent per hour Two thirds of injected radiothyroxine was ultimately excreted in feces and one third in urine Thyroxine or some derivative of it was slowly removed from blood by fixation in tissues particularly the liver Such fixation also occurred in kidney and in other tissues at a rate of about

equilibrated with serum iodide and is present as only a small percentage of the total serum iodine partly because it is disposed of rapidly and partly because its volume of distribution is comparatively large. The liberated iodide present in blood is eliminated mainly in the urine. Thyroid hormone is not accumulated by the thyroid and reutilized. Iodide liberated in the catabolism of thyroid hormone is reaccumulated and reutilized in a normal person. Approximately 20 per cent of the liberated iodide would be accumulated by the normal thyroid. The iodide of dietary origin probably accounts for far more of the iodide utilized by the normal thyroid for synthesis of new thyroid hormone than does the small porportion of iodide liberated from the catabolism of thyroid hormone which is reaccumulated.

In a later study,[87] radiothyroxine was injected intravenously as a single dose in 6 patients with exophthalmic goiter. The initial phase of disappearance from the blood was very rapid, with a half-value time of 3 hours. After 12 or more hours a slow disappearance with a half-value of 5 to 6 days became apparent, presumably due to utilization of the thyroxine by the tissues and excretion in the urine and feces. Uptake by the thyroid and excretion in the urine after administration of radio-thyroxine were slower than after administration of radio-iodine and appeared to depend for the most part on the rate of release of radio-iodine from radiothyroxine. In these patients, too, the main metabolic fate of thyroxine, aside from some excretion in the feces and the urine, was de-iodination. Part of the iodide thus released was reaccumulated in the thyroid and part was excreted in the urine, depending upon the ratio of the thyroidal clearance and the renal clearance. About one third of the injected hormone was metabolized in 24 hours.

The physiological effects of the hormone will now be considered in detail. The differential analysis of its effects should not obscure the fact that in the patient the actions are multilateral and simultaneous, involving many tissues and organs.

Oxidative and Calorigenic Action

The first observation of the calorigenic effect of thyroid was made by Magnus Levy in 1895, when he demonstrated that thyroid deficiency was associated with a reduced metabolism and lowered oxygen consumption.[88] The fundamental oxidative processes of the body and minimal heat production are cellular phenomena which proceed independently of

treatment with thyroglobulin produced a marked increase in thyroidal I 131 and a marked and asymmetrical decrease in the extrathyroidal I 131, a greater decrease occurring in the gastro-intestinal tract than in the carcass Thus there exists a wide range over which the excretion of I 131 from the body is proportional and in equilibrium with the secretion or loss of I 131 from the thyroid When liberation of thyroidal I 131 is inhibited by therapy with thyroglobulin, the excretion of I 131 in feces and urine is correspondingly inhibited However when liberation of thyroidal I 131 is accelerated by thiouracil, the fecal and urinary excretion of I 131 is also accelerated but does not keep pace with the liberation of I 131 from the thyroid There appears to be a ceiling beyond which the body cannot further excrete labeled thyroid hormone

Klitgaard,[87f] on the other hand in studies of the biliary and urinary excretion of radio iodine following subcutaneous injection of tracer amounts of I 131 labeled thyroxine in normal hypothyroid and hyper thyroid rats found that thyroidectomized and thiouracil treated groups showed reduced biliary radio-iodine elimination as well as diminished bile volume during the 6-hour collection period Hyperthyroid animals showed a marked increase thiouracil-treated animals a decrease in urinary excretion of radioactive iodine over a 12 hour period The radio iodine excretion in both bile and urine tended to be lower in the thiouracil-treated rats than in the thyroidectomized groups

The metabolism of thyroxine has also been studied in human subjects with normal decreased and increased thyroid function[87g, 87, 87, 8j] Albert and his associates[87, 87] have studied the metabolic behavior of racemic radiothyroxine administered orally or intravenously to patients with myxedema maintained in a euthyroid state with non labeled racemic thyroxine Forty-one per cent of the radioactivity was excreted in the urine and 12 per cent in the feces Eighty five per cent of the urinary I 131 was present as inorganic iodide and 15 per cent as organic I 131 consisting of both thyroxine and diiodotyrosine The bulk of thyroid hormone is therefore de-iodinated and excreted in the urine as iodide On the basis of these studies Albert and his co workers formulated the *following highly tentative picture of the metabolism of thyroxine under* normal conditions On entry into the circulation thyroxine is confined at first to the plasma from which it is transferred to the tissues of the body including especially such organs as the liver and becomes equilibrated with the thyroid hormone already present in tissue In the tissues thyroid hormone is catabolized mainly to iodide and to a minor extent is split apparently at its ether linkage The iodide liberated becomes

The calorigenic action of the thyroid hormone has been clearly traced to the tissues but the exact mechanism by which it alters metabolic processes is unknown It is probably not a true catalyst because it lacks uniformity of effect among various tissues and because its effect is delayed in appearance Both Gordon and Heming and earlier Dye[93] suggested that it works by increasing the effectiveness of or by stimulating the synthesis of various respiratory enzymes

Thyroid in Thermoregulation

In its oxidative function the thyroid contributes significantly to total heat production In addition the gland has a definite relation to the actual regulation of the body temperature Prolonged exposure to cold results in increased thyroid activity [94] This has been most satisfactorily demonstrated by measuring the fixation of radio iodine in the rat s thyroid following exposure to varying temperatures[95] Exposure to freezing temperatures (0 to °) produced thyroid stimulation after 7 days which reached a maximum after 26 days and was absent after 40 days There was a nearly threefold increase in the uptake of radio iodine for thyroxine synthesis at the time of maximal stimulation by the cold Heat lessened thyroid activity but the effect of heat was far less prominent than that of cold

The thermoregulatory function of the thyroid is dependent upon both the hypophysis and the adrenals According to Uotila[96] hypophysectomy abolishes the response of the thyroid to cold Epinephrin has a calorigenic effect which is greatly increased by the thyroid hormone[94] Dinitrophenol in amounts calorigenically equal to thyroxine increased the hypothermia of mice subjected for 1 hour to an environmental temperature of 5 C whereas thyroxine decreased such hypothermia[97]

The role of the thyroid in thermoregulation is also reflected in changes in the gland occurring seasonally Riddle[98] found the thyroid of pigeons to be larger in winter and smaller in summer Earlier Seidell and Fenger[99] demonstrated a threefold increase in iodine content of the thyroid gland of various animals during the summer months thus indicating reduced physiological activity Kendall and Simonsen[100] similarly found increased iodine and thyroxine content of the gland during the summer and a decrease during the winter Dempsey and Astwood[101] have determined the rate of hormone secretion at various environmental temperatures by measuring the amount of thyroxine

thyroid activity but the thyroid in the words of Marine 'provides the means through its iodine containing hormone of maintaining a higher level of metabolism than would otherwise obtain [89] In other words the thyroid forces an increased rate of oxidation within the cell There is production of heat with oxidation and thus the oxidative effect of thyroid is known as its calorigenic action

The calorigenic action of thyroid may be readily measured in the organism by the determination of oxygen consumption or carbon dioxide production This is the method of indirect calorimetry and is the basis of clinical metabolism testing wherein the oxygen consumption is measured for an exact unit of time and compared with standard values for normal individuals One may however with a calorimeter measure the heat production of the organism by utilizing the method of direct calorimetry this is too cumbersome for clinical purposes but has been of fundamental importance in research on energy metabolism

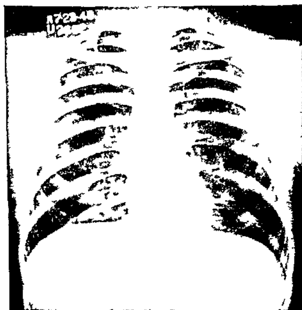
In the resting-fasting state the thyroid accounts for slightly less than half of the total heat output or oxygen consumption since total thyroidectomy or myxedema decreases the basal metabolic rate by about 40 per cent The organism lives and respires but the oxidative fires burn low

That the thyroid hormone produces its calorigenic effect by direct action on the tissues or the tissue cells has been established in many ways Aub and his associates [90] showed that the hypermetabolism induced by thyroxine could not be explained by muscular activity or tonus and was unaffected by adrenalectomy Studies on the whole animal because they are complicated by nervous and interhormonal relationships have to some extent been supplanted by observations on excised organs or tissues in further efforts to understand the exact way in which the thyroid exerts its oxidative effect

Myer McTiernan and Aub [91] showed that liver slices from thyroxinized mice had an increase in oxygen consumption and in anerobic glycolysis They also demonstrated that the oxygen consumption of denervated and normal kidneys is similar in thyroxinized dogs The nervous system is thus not essential for the effect of thyroxine on tissue metabolism The direct effect of thyroxine upon tissues is not universal since these same workers found no effect or a depressing effect on the oxygen consumption of malignant tissues excised from thyroxinized mice In similar fashion Gordon and Heming [9] found that administration of thyroid and thyroxine caused significant increases in the oxygen consumption of liver, kidney diaphragm and heart of the rat but they observed no effect on spleen brain or testis



A



B

FIG 2 A comparison of the appearance of the heart shadows in roentgenograms of two individuals without heart disease who died noncardiac deaths and who showed at autopsy heart weights of 200 grams each without any evidence of cardiovascular abnormalities

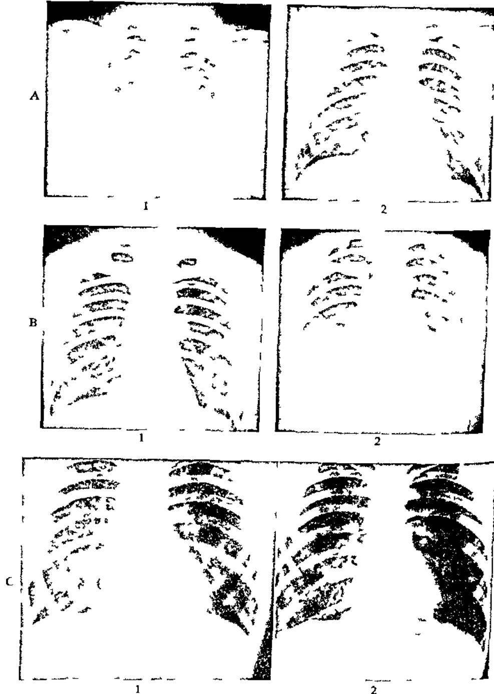
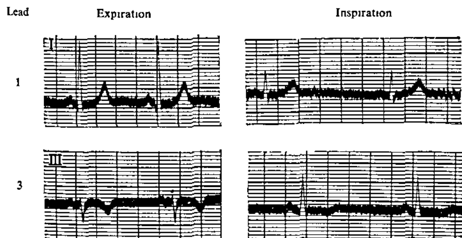


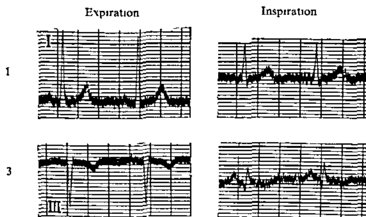
FIG 3 Roentgenograms of the thoraces of normal young men showing the effects on the heart shadows of alteration of the level of the diaphragm in respiration (*A*) Short stocky physician (1) during quiet breathing in upright po ition (2) at height of full inspiration in upright position (*B*) Slender young physician (1) during quiet breathing in upright position (2) at height of full expiration in upright position Note the similarity of *A*1 and *B*2 and of *A*2 and *B*1

(*C*) B W male age 27 (1) Normal control deep inspiration immediate exposure T D 14 6 cm height of diaphragm 13 1 cm (2) Effect of Valsalva s experiment deep inspiration followed by forced expiration against 40 mm Hg for 5 second T D [illegible] cm height of diaphragm 12 4 cm T D = transverse diameter of heart

often deposited in the abdomen or in its wall certain intra abdominal diseases particularly resulting in enlargement of liver or spleen ovarian cyst or ascites diaphragmatic herniation and finally with certain intrathoracic diseases especially those that cause an extreme pulmonary emphysema with deep lowering and little motion of the diaphragm It is often not realized that the prolonged fixation of the diaphragm at the level of full held inspiration (simu lating the Valsalva experiment) results in an appreciable decrease in the size of the x ray heart shadow (Figure 3C) this can result in erroneous estima



A



B

FIG 4 Electrocardiograms (Leads 1 and 3) from two normal individuals (*A*) and (*B*) showing the effect of deep expiration and inspiration on the deviation of the electrical axis

tion of heart size if roentgen studies of the lungs are used for cardiac appraisal (see Chapter 7)

Besides the height of the diaphragm the position of the body itself makes a difference (Figure 6) One should always stipulate therefore whether an examination physical x ray or electrocardiographic is made in the upright position or recumbent In our own cardiographic laboratory years ago w

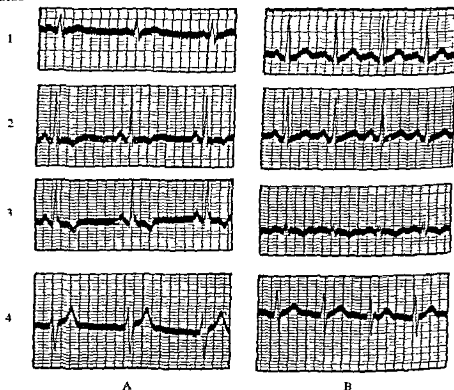
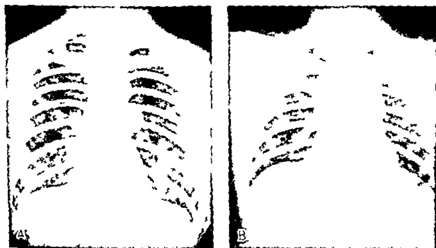


FIG 5 Electrocardiographic changes (4 leads) with respiration in normal healthy man of stocky build (*A*) At height of full inspiration (*B*) At height of full expiration Lead 4 was taken with exploring electrode over the fifth intercostal space at the lef midclavicular line and the remote electrode on the left leg (Graybiel and White *Electrocardiography in Practice* W B Saunders Company Philadelphia 1941 Figures 16 and 17)

didn t record the position although the tracings were almost always made with the patient sitting comfortably In the last ten years however since we found what a difference position may (though it usually does not) make we have recorded by a simple straight line the angle of the patient s body Po i tions of diaphragm and of body influence not only the anatomic and electric angle of the heart in the frontal plane but result in a rotation which is also important in its effects though not so easy to measure

The immediate state of health is another vital factor frequently influencing the heart findings on examination A heart perfectly normal to start with

and even later on showing normal myocardium endocardium valves and pericardium at autopsy may dilate acutely or subacutely from the effect of severe hypochromic anemia massive pulmonary embolism (to produce the acute cor pulmonale) and paroxysmal tachycardia at excessive rates as for example in the case of infants where the heart rate may reach 300 or more a minute and result not only in general cardiac dilatation but also in congestive failure with engorgement of the liver Some of these infants have been erroneously diagnosed as having the so-called idiopathic hypertrophy of the heart and some have been wrongly regarded as abdominal emergency



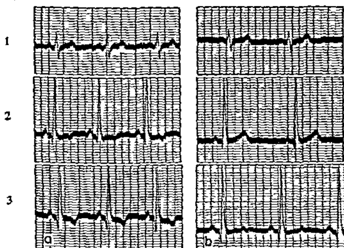


FIG 6 Roentgenograms of the thorax of a healthy young man (above) and electrocardiograms (limb leads) of another healthy young man (below) both slender in build showing the effect of change in body (and heart) position—(*A* and *a*) sitting upright (*B* and *b*) lying supine

cases for example pyloric stenosis because of the vomiting caused by the acute congestive failure Severe infectious diseases may also alter the presumably normal cardiac findings on examination without producing actual heart disease Acute rheumatic infection can of course precipitate acute or subacute cardiac dilatation and failure from the rheumatic myocardial disease, and diphtheria may seriously affect the myocardium but leaving these two specific infections out there are still other infections like pneumonia which may cause temporary systolic murmurs and even electrocardiographic changes especially in rapidly growing or delicate individuals Whether these murmurs are to be ascribed always to slight dilatation or how much the speeding up of blood flow has to do with them we don t know It is clear however that thyrotoxicosis without producing actual heart disease in the acute cases can alter the findings on examination of the heart not only in producing a tachycardia and increased pulse pressure but by the increased pulmonary blood flow causing marked accentuation of a physiologic pulmonary systolic murmur and a bulging of the pulmonary arc in the x ray picture simulating a mitral shape of heart shadow

How much the factor of physical strain is responsible for changes in heart size and shape in man we don t know Once upon a time the medical profession as well as the laity talked glibly of the athletic heart When most athletic hearts were shown to be something else the term went into the discard and now we doctors say almost as glibly that there is no such thing as an athletic heart However a revision of the past and present opinions is still awaited on the basis of most careful studies not yet adequately assembled There is a hint from several sources including an annual appraisal of Harvard oarsmen which was for some years conducted by various associates of mine that an occasional or more likely a rare person may after some years of excessively strenuous sport develop an increase in heart size out of keeping with any increase in body size This sort of change is reasonable to expect in view of experimental evidence in animals where it has been shown that long-continued physical exercise produces hearts that are distinctly larger than those of animals kept very quiet and in view of the well known fact that hares have relatively very much larger hearts than have rabbits racing greyhounds than other dogs and race horses than ordinary mounts Exercise can of course produce transient systolic murmurs mostly in the pulmonic area or increase those already present even in normal persons Another point of interest is that a trained athlete tends to have a slow pulse or one that slows quickly after exercise although I can well remember counting the pulse rate of the winner of a marathon race a few years ago and finding it faster (118) at the starting line before he had taken a step than at the finish (110) after running 26 miles in his case nervous tension as to the outcome of the race was doubtless responsible acting like stage fright I would hasten to add however that there is no evidence that vigorous exercise in the case of a healthy person in good training hurts the heart If anything the reverse is true as pointed out by Morgan in a volume entitled *University Oars* published by

Macmillan in London in 1873 in this book data are presented which indicate that the Cambridge and Oxford oarsmen of a hundred years or more ago outlived their expectation It may well be that the change to a very sedentary life is more harmful than a maintenance of exercise

The effect of high altitude on the heart and circulation is in rare individuals an important consideration Not many persons have exposed themselves to altitudes of 12 000 feet or more as permanent residents or even temporarily but now of course with the circulatory adjustments in aviators especially in military service the problem has become acute Circulatory collapse probably antedates serious cardiac involvement itself in mountain climbers and in aviators in the latter either from the effect of low oxygen tension in the atmosphere or from the centrifugal force of great speed and change in direction or from still other factors Residents at very high altitudes do however show circulatory adjustments that have been well described and resemble somewhat those in the cyanotic type of congenital heart disease at sea level Tandler has pointed out incidentally that the bird Lagopus living in the Alps has a heart weight 50 per cent greater than that of the Lagopus of the same size living at lower altitudes

The factor of the effect of rapid growth on cardiac findings has not yet been completely assessed It is the impression of many of us that a fast growing boy or girl or indeed a delicate child of any age is very prone to show an instability of circulation and heart action and easily induced heart murmurs from fatigue overexertion or mild infection that do not signify the presence of heart disease or active rheumatism which we are so prone to suspect in our climate in New England and rightly so of course in many cases We need more enlightenment in this problem

I have already referred to pregnancy as a factor which alters the height of the diaphragm and so affects both x ray picture of the heart and electrocardiogram but it has other results too Through the influence of the increased blood volume and circulation the heart volume is itself somewhat increased and pulmonary and even apical and aortic systolic murmurs may appear due in part to such factors and in part to the upward displacement of the heart and great vessels

Still further factors significantly affecting the action of the normal heart are the emotions as pointed out by the ancients and restated by Williams Not only may fear and pain alter heart rate blood pressure heart sounds and subjective sensations but through action on the sympathetic and parasympathetic nerves they may even alter the electrocardiogram With tachycardia the *T* waves are often depressed and on occasion excessively so even inversion of the *T* waves has been induced by sudden fright as it has been also but doubtless through a different mechanism by drinking ice water

And finally we come to the toxic influences of drugs or poisons on the normal heart Those that are best known are the effects of digitalis atropine and quinidine but there are doubtless less well known drug actions or the influence of rare poisons that need exploration This is an important digres-

sion for toxic effects on an otherwise normal heart may simulate serious disease as was so well borne out in the famous insurance racket in New York City some years ago when a few crooked doctors lawyers and insurance clients conspired to defraud the companies by the production of ill health and electrocardiographic changes by large amounts of digitalis these symptoms and signs being attributed to coronary disease I myself have taken experimentally, moderate to large doses of digitalis and have not only altered my electrocardiogram with lengthening of *P R* intervals and depression of *S T* segments and *T* waves and induced anorexia and nausea but also caused disagreeably forceful heart action at an ordinary rate as well as extrasystoles and paroxysms of tachycardia Atropine while producing tachycardia lowers the *T* waves of the electrocardiogram as well as does the inhalation of tobacco smoke epinephrine (adrenaline) lowers and may even invert the *T* waves in Lead 2

In later chapters I shall take up in some detail the actual measurements anatomic and physiologic that are considered to be within the range of the *normal heart blood vessels, and circulation and shall also in later chapters* discuss symptoms and signs that may be the result of either cardiovascular diseases or of other factors not related to such diseases There still tends to be *overdiagnosis of heart disease by the erroneous application of both sub*jective and objective data I have spent almost as much time in correcting wrong diagnosis of heart disease based on normal variations as I have in *establishing or confirming the presence of actual heart disease One of the* most common of all errors is that of including a large triangle of fat at the cardiac apex as a part of the heart shadow in roentgenologic cardiac mensuration (Figure 7)

In concluding this chapter I have still another observation to make closely related to the present subject and fundamental It may well be the most important thing I shall have presented in this book It is doubtless often a subject of thought but there has been surprisingly little reference to it especially as it relates to the heart Can we tell when an organ is strictly normal? After all what is normal? The word comes from the Latin norma which means rule pattern or carpenter s square Normal health is supposed to be a state of the body in which disease is not discoverable May there not be a few grams of increase in heart weight from one strain or another without lack of ease or objective evidence resulting? May there not be quite extensive change in the coronary arteries of many of us even with narrowing and perhaps small or gradual symptomless occlusions here and there with no lack of ease and with perfectly normal electrocardiograms? And we may have to be run over at ninety or die of pneumonia which proves resistant to chemotherapy Are these coronary changes even if they do produce electrocardiographic abnormalities in old age to be regarded as disease or may they not be considered like gray hairs as a part of the natural process of growing old? When does natural aging stop and disease begin? I find incidentally a great help in using this conception in talking to patients who are going through an acute or chronic

process of adjustment of their coronary circulation with coronary insufficiency so often a temporary state lasting but a few weeks or months or a year or two It is a comfort for the patient to realize that there is not actually a 100 per cent difference between his coronary arteries and those of his friend who feels perfectly well there may be only 3 or 4 per cent He himself may be just over the threshold of clinical evidence and his friend just under

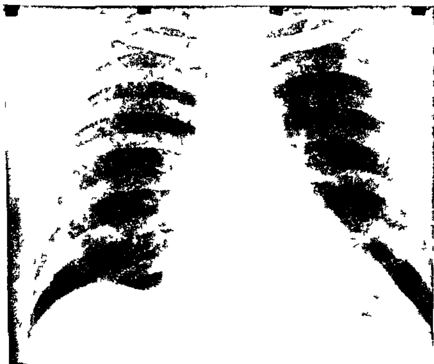


FIG 7 Roentgenogram of healthy fat man showing a large triangle of epicardial fat at the pericardiodiaphragmatic angle on the left a common source of error in estimation of heart size

In summary then let me repeat that we need much more study of normal controls than we possess at present of the heart in all types of mankind and by all methods of examination especially x ray analysis and electrocardiography In the past we have all rushed to what has seemed more interesting and exciting namely the evidence of diseased states so that actually at the present time we are likely to be more thrilled by separating from the category of manifestations of disease certain normal findings than we are to discover disease itself We have put the cart before the horse but it is not too late to change about In the study of pulse rate and blood pressure range we do now have normal standards based on hundreds of thousands of individuals but there is still some uncertainty as to interpretation of borderline readings especially of those in the upper range how high for example may blood pres

sure readings, both systolic and diastolic rise in a normal person from nervousness alone? We need many thousands of normals for x ray heart measurements and electrocardiograms and at the same time better correlations with body build so that we may construct more accurate tables always avoiding however blind worship of formulas and figures Even statistical analysis helps us but little here for there is still a chance that an individual with measurements at the outer range of normal among thousands of carefully studied cases may himself or herself be either healthy or diseased

Hence until we acquire adequate information and even when we have it we can save ourselves a lot of worry and uncertainty as to whether any given individual has acquired an abnormality of the heart by following Floyer's advice and making a careful routine examination including x ray film and electrocardiogram while the subject is still in excellent health A comparison of serial data on a given person is more valuable than checking him or her against any standard tables

Finally when all is said and done the borderline between the perfectly normal and the slightly but definitely abnormal is so wide not only clinically but anatomically as well that it is unlikely that we can ever draw a sharp line between them nor should we try too hard so to do

BIBLIOGRAPHY

INCLUDING GENERAL REFERENCES ON CARDIOVASCULAR DISEASE

Clark A J *Comparative Physiology of the Heart* Cambridge University Press New York 1927

Corvisart J N *Essai sur les Maladies et les Lesions organiques du Coeur et des gros Vaisseaux* Migneret Paris 1806

Floyer John *The Physician s Pulse Watch* Sam Smith and Benj Walford London 1707

Hillman C C Levy R L Stroud W D and White P D Studies of Blood Pressure in Army Officers Observations Based on an Analysis of the Medical Records of 22 741 Officers of the United States Army *J A M A* 1944 CXXV 699 and CXXVI 829 1945 CXXVIII 1059 and CXXIX 585 1946 CXXXI 951 1947 CXXXV 77

Morgagni J B *De Sedibus et Causis Morborum* Typographia Remondiniana Venice 1761

Morgan J E *University Oars* Macmillan & Co Ltd London 1873

Smith H L The Relation of the Weight of the Heart to the Weight of the Body and of the Weight of the Heart to Age *Am Heart J* 1928 IV 79

Tandler J *Anatomie des Herzens* Gustav Fischer Jena 1913

Vierordt H *Anatomische physiologische und physikalische Daten und Tabellen zum Gebrauche fur Mediziner* Gustav Fischer Jena 3rd ed 1906 (1st ed 1881)

Wiggers C J *Modern Aspects of the Circulation in Health and Disease* Lea and Febiger Philadelphia 2nd ed revised 1923 (1st ed 1915)

Williams John C *Practical Observations on Nervous and Sympathetic Palpitation of the Heart Particularly as Distinguished from Palpitation the Result of Organic Disease to Which are Prefixed Some General Remarks on the Use of the Stethoscope and Employment of Percussion in Diagnosis of Diseases of the Heart and Lungs* Longman Rees Orme Browne and Co London 1836

CHAPTER 3

THE PATIENT'S HISTORY AND SYMPTOMS

The present chapter and the next after careful scrutiny as in the case of Chapter 2 have required but minor changes They may I hope continue to be helpful especially to those not already expert in the field of cardiology and to those more experienced who have become careless or hurried in their history taking and physical examinations and who are still too numerous

THE PATIENT'S HISTORY

The diagnosis and treatment of heart disease are dependent upon the history and examination of the patient The capacity to elicit the significant symptoms and signs the ability to analyze these symptoms and signs after they have been found the knowledge of the best therapy and not the least important of all the quick appraisal of the sort of person to be treated are all essential to the satisfactory practice of medicine In one s early days in medicine in school and for a while afterward the analysis of symptoms and signs and to a lesser extent their treatment may be learned with a fair degree of success the ability to elicit the symptoms and signs and the understanding of the individual patient and his reactions are taught less easily by word of mouth or book but come gradually with experience Without this experience in practice one may continue but half trained although able to discourse learnedly on diagnosis and treatment No amount of reading or discussion can take the place of prolonged hard work in the clinic or in the homes of patients the science of medical practice cannot be taught in the classroom

It is therefore impossible for me to do more in this discussion of examina tion and of symptoms and signs than to point the way and to trust that eventually proficiency may come to each individual who rounds out with his own experience such information as he may find in this and other books Any physician may and doubtless will discover in time innovations or modifica- tions of our present methods of examination and analysis whereby the study and treatment of cardiovascular disease can be furthered Progress in the last generation has been rapid and has been advanced at a fast pace in the last twenty years since the publication of the first edition of this book We have at hand a far better chance to diagnose and to treat heart disease successfully

than had our fathers and there is no reason why this march should not continue With our wealth of methods of examination however there is danger that we may become overconfident or neglectful Sometimes physicians tend to abandon old and tried methods for the new while at other times they shun new and useful methods because they fear they are but transient or because they cannot or do not want to take the time to master them or even to understand them But often diagnosis is so difficult and signs are so misleading that we must make use of all the best tried methods at our disposal before we have properly dealt with a difficult case

In the first part of the book which takes up the examination of patients I shall discuss briefly the methods that have proved valuable and shall have little to say about other methods of less or of doubtful value I shall also discuss the results of these examinations that is the analysis of symptoms and signs, reserving for later parts of the book a detailed consideration of the causes significance and treatment of the cardiovascular conditions revealed by these symptoms and signs

First and most important of all is the story of the patient himself together with a careful consideration of his personality and reactions as he tells his own story If told by someone else especially in the absence of the patient the story has a certain amount of value dependent on the narrator s intelligence and the closeness of his acquaintanceship with the patient but this procedure prevents insight into the case that may come only by listening to the patient s own discussion of his history and symptoms It has been my custom in private practice to allow a full half hour and sometimes longer for the new patient s history except in very simple or special cases I am convinced that this time has been more profitably spent than that of any other part of the examination Not only has it revealed direct information often of great value but it has indirectly revealed knowledge of the type of person recounting his history and most important of all it has almost invariably secured the sympathetic cooperation of the patient Detailed and careful history taking is bv no means the general rule It is to be sure, sometimes difficult or impossible in general practice but even when possible it is frequently neglected more I believe in Europe than in the United States Its cultivation is worth serious effort and should not be left to a secretary or assistant It is better to rely on an assistant s physical examination than on his history taking if both cannot be accomplished by oneself I have also found it best for the trained physician to take his own notes of the history during the interview this is preferable to dictation to a secretary or assistant whose presence tends quite naturally to act as a check on free discussion

The patient s history had best begin with a very detailed account of the present illness but under no condition should it be left at that In some cases to be sure it may be necessary temporarily to postpone the rest of the history because of fatigue or serious illness or for another reason but it is essential to remember that significant clues or guides to diagnosis prognosis and treatment may rest in the past history of illnesses operations or accidents in the

opinions or treatment of other doctors (often neglected especially by hospital internes) in the social and occupational history in the account of the patient s habits and last but not least especially from the viewpoint of prognosis, in the family history another frequently neglected source of information

SYMPTOMS

The personal story of the exact onset of the very first heart symptom should be the foundation stone on which the examination of the cardiac patient rests One sentence accurately and adequately presenting this information may be more valuable than all the other data put together An error or vagueness at the beginning may be seriously misleading It is important to remember that not only may cardiac symptoms be confused with noncardiac symptoms but even when cardiac symptoms pain dyspnea and palpitation are actually present they may be confused with each other as in a case of paroxysmal tachycardia wrongly diagnosed angina pectoris or of angina pectoris wrongly labeled breathlessness because of hasty questioning The development of the first symptom its evolution and the appearance of other symptoms must be carefully recorded according to date circumstances character intensity variability and relationship in order to gain full advantage from all available clues

Symptoms are dependent on two primary factors (1) stimulation of sensory nerves and (2) sensitiveness of the nervous system The percentage of responsibility of each factor must be judged in every case it is constantly varying even in the same case at different times Thus a relatively insensitive nervous system may give rise to no symptoms even when there is apparently considerable cause for stimulation while a sensitive nervous system may produce symptoms with very little stimulation If fatigue lowers the threshold of the relatively insensitive nervous system symptoms may be produced by stimulation which before was ineffective if rest raises the threshold of the sensitive nervous system symptoms may no longer be caused by the stimulation heretofore effective

Symptoms do not mean disease they indicate temporary disturbance of function whether or not dependent on structural pathologic changes

I shall consider first the three most important symptoms of cardiovascular origin—pain respiratory disorders and palpitation—and after that a group of less important symptoms

Pain (ποινη penalty) **of cardiovascular origin** In the first place it must be realized that pain in the chest may or may not be caused by trouble with heart or great vessels and that heart trouble may be responsible directly for pain that is outside the chest (referred pain) even when there may be no simultaneous chest pain There are still obscurities about the transmission and interpretation of sensory nerve impulses from the heart but an increasing interest in the autonomic nervous system in the last two decades gives promise of clearing away many of the problems (White J C 1935) It has for example

been demonstrated in recent years that cardiac pain is carried to the central nervous system by the first four or five dorsal rami communicantes on each side by way of the corresponding ganglia from the first (stellate) down and not by way of the cervical sympathetic chains and stellate ganglia alone

Before proceeding to the kinds of heart and great vessel pain, it is important to emphasize that discomfort due to breathlessness or palpitation is not to be called pain although it is true that actual pain may accompany breathlessness or be induced by heart action responsible also for palpitation

Thoracic pain for which heart and great vessels are responsible is best discussed under seven headings (1) precordial aching or heartache, and short sharp stabs of pain (2) substernal oppression either transient (lasting a few minutes) as in the case of paroxysmal angina pectoris or of longer duration (lasting often for hours) as in the case of acute coronary occlusion (3) angina hypercyanotica (4) the pain of acute pericarditis (5) the pain of acute rheumatic carditis (6) pressure pain from aortic aneurysms and (7) the tearing pain of dissecting aneurysms of the aorta Whether pain results from the acute cor pulmonale per se is as yet problematic because of the presence of the underlying acute pulmonary embolism which may itself produce great distress in the anterior thorax or induce coronary pain in a patient who already has considerable coronary artery narrowing or cause pain from the resulting pleuropulmonary infarction An interesting and important cardiac cause of *right upper quadrant abdominal pain* is acute engorgement of the liver with stretching of its capsule secondary to abrupt failure of the right ventricle it may occur paroxysmally on effort (Boyer and White 1942) The most common or important noncardiac causes of substernal or anterior chest pain to be differentiated from the types described above are spasm of esophagus or stomach (cardiospasm) sometimes with hiatus hernia pleurisy muscle and joint discomfort neuritis herpes zoster mediastinal or other intrathoracic tumors pneumothorax and mediastinal emphysema and neurosis

1 *Precordial aching* or *heartache* maximal as a rule in the center of the left breast is the commonest kind of heart pain It may be very mild moderate or very severe and wax and wane for hours to years rarely does it last as short a time as a few minutes on any one occasion When severe it may radiate all over the anterior thorax and even into the arms especially down the left arm in such cases it is easily mistaken for angina pectoris Also when it is severe it is often accompanied by precordial tenderness which is a vitally important clue to the proper interpretation of the heartache itself The essential cause of this kind of pain is oversensitiveness of the nervous system from fatigue or other factor it is characteristic of the majority of cases of neurocirculatory asthenia (see Chapter 22) If it is found in the presence of heart disease itself it is to be interpreted only as a complication and not as a direct result of the heart disease it is however true that the larger the heart and the more forceful its action the more likely are heartache and precordial tenderness to be present The pathogenesis is probably that of the thumping of the heart whether normal or diseased against an oversensitive thoracic wall

Short sharp stabs of pain in the precordium are to be fundamentally explained in the same way as is precordial aching, the immediate cause of such a stab as if from a pin a needle or a knife is in many cases a premature beat or extrasystole

Thus heartache and precordial stabbing sensations are unimportant and in fact often reassuring so far as serious disease is concerned the majority of patients showing such symptoms have no heart disease at all The idea once expressed that myocardial fatigue in chronic heart disease may produce these symptoms has not been borne out in the studies of the last decade or more An interesting observation concerning the *side ache* that not infrequently occurs in either left or right upper quadrant of the abdomen on exertion in normal persons has been presented by Capps (1941) he ascribes this ache to anoxia of the diaphragm on either side

2 *Substernal oppression dependent on coronary insufficiency* is also common but it is of far greater significance than heartache so far as prognosis is concerned It may be mild moderate or severe and may or may not show transmission of pain to arms neck jaws or back Many times heartache of no importance is more severe than angina pectoris of great importance The substernal oppression is almost invariably the result at first of considerable effort under special circumstances such as hurrying for a train on a cold morning in fall or winter directly after breakfast in comparison to the heartache of neurocirculatory asthenia which occurs at any time especially when fatigue sets in at the end of the day Substernal oppression dependent on coronary insufficiency is usually at first paroxysmal lasting but a few minutes at a time as such it has been called angina pectoris (see Chapter 21) When it lasts for hours it is due most commonly to myocardial infarction resulting from acute occlusion of one of the main coronary arteries or branches in almost all cases the result of thrombosis on an atherosclerotic background but in rare cases due to embolism (see Chapter 21) Tenderness over the sternum in cases of substernal oppression does not occur unless there is a complication of neurocirculatory asthenia Actual coronary disease atherosclerotic or otherwise is fundamentally responsible for the large majority of all cases showing substernal oppression dependent on coronary insufficiency in a few cases other factors such as syphilitic aortitis anemia or possibly even coronary spasm itself are wholly or in major part responsible

Sometimes the site of angina pectoris is a little to the left of the sternum (rarely to the right of the sternum) rather than directly substernal very infrequently is it in the middle of the left breast where the more prolonged heartache described above is located and rarely does coronary insufficiency give rise only to referred pain in one or both arms hands or jaws without substernal oppression—in such cases the greatest care and judgment are necessary in its interpretation

3 *Angina hypercyanotica* is rare A heavy pain precordial and substernal with or without radiation is felt by some individuals who have considerable cyanosis especially by a few with marked mitral stenosis or massive pulmonary

embolism and is due probably to myocardial anoxia it has been called angina hypercyanotica

4 *Heart pain of acute pericarditis* is not common The majority of cases of pericarditis acute or chronic have no pain but if there is involvement of certain parts of the parietal pericardium in particular that adjoining the pleura or outer diaphragmatic portion of the pericardial sac there may be disagreeable pain resembling that of pleurisy and usually aggravated by respiration (Capps 1927) the fact that the pain of pericarditis is almost always much increased by the act of inspiration is a very important clue in distinguishing it from the pain of myocardial infarction with which otherwise it may easily be confused The pain originating in the diaphragmatic pericardium tends to be referred to the left shoulder An acute pericardial effusion may cause a vague dull precordial oppression

5 *Heart pain of acute rheumatic carditis* consists of precordial pain sharper than that of the heartache of neurocirculatory asthenia but not so sharp generally as the pain of acute pericarditis although it may complicate the latter It recurs as a rule for a few days during a severe rheumatic infection in childhood It is not a constant finding Its pathogenesis is not clear

6 *Aortic aneurysm pressure pain* is a severe more or less constant ache in upper thorax neck or shoulder dependent on pressure of the growing aneurysmal sac against surrounding tissues especially bones cartilage and nerves it usually requires morphine or alcohol injection of nerves (see Chapter 28)

7 *The pain of a dissecting aortic aneurysm* is usually excruciating and tearing located substernally or in the back and radiating through the chest from back to front or vice versa and often down the back to the legs It tends to be at its height at the very outset in contrast to the pain of coronary occlusion which takes a few minutes to work up to its severest intensity It lasts for hours and usually ends in death due to secondary rupture of the aorta into pleura pericardium, or elsewhere It is due to the extensive tearing of the media of the aortic wall often through its entire length from aortic valve to bifurcation at the common iliac arteries and in large part circumferentially also It is likely to be confused with the pain of acute coronary occlusion (see Chapter 28)

Disorders of respiration There are only three fundamental disorders of respiration that are related to heart disease itself These are (1) dyspnea that is difficult breathing (2) cardiac asthma and (3) periodic apnea and hyperpnea or the so-called Cheyne Stokes respiration Rapid breathing (tachypnea without dyspnea) slow breathing (bradypnea) and sighing respiration are not directly related to heart disease although they are sometimes so misinterpreted particularly the last named Sighing is an important clue when excessive to neurocirculatory asthenia which may or may not complicate heart disease (Figure 8 and Chapter 22)

1 *Dyspnea* (δυσ difficult and πνοη breathing) is of course not pathognomonic of heart disease it has many other causes chiefly pulmonary dis

eases acute and chronic pleurisy with and without effusion bronchial asthma diseases or obstruction of the upper respiratory tract larynx and trachea mediastinal diseases diaphragmatic hernias and certain nervous affections The dyspnea produced by heart disease is mainly the result of a reflex action on the respiratory center from engorgement of the pulmonary circulation Such pulmonary vascular congestion is produced most commonly by failure of the left ventricle and less commonly by the obstruction due to mitral valve deformity (stenosis regurgitation or both) sometimes wrongly interpreted as

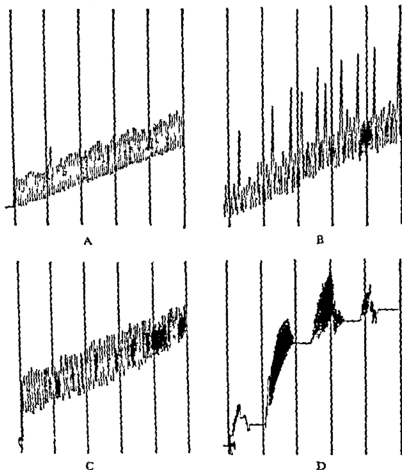


FIG 8 Spirograms showing several types of respiration (*A*) Normal respiration over interval of 5 minutes Inspiration shown by upstroke and expiration by down stroke Respiratory rate = 14 to 16 per minute Time interval 1 minute (*B*) Sighing respiration in case of neurocirculatory asthenia without heart disease Ten sighs are recorded in the interval of 5 minutes Respiratory rate = 12 to 15 (*C*) Dyspnea due to congestive heart failure Note increase in respiratory rate from 14 to 22 toward the end of 5 minutes at which time it was necessary for the patient to change from the supine to the erect position Note the absence of sighing respiration (*D*) Cheyne Stokes respiration The durations of the three hyperpneic phases which are completely shown are 50 55 and 30 seconds respectively and of the three apneic phases 40 35 and 30 seconds respectively

the result of failure of the right ventricle Actual effusion of edema fluid into the pulmonary alveoli in some cases undoubtedly adds its effect in exaggerating the dyspnea probably chiefly through stimulating the respiratory center by the oxygen lack and increased carbon dioxide in the blood Failure *of the right ventricle with resulting stasis and disturbed gas content of the* blood supply to the respiratory center is another cause of cardiac dyspnea but less common and later in appearance Many cases with right ventricular failure constrictive pericarditis or tricuspid stenosis and elevated venous pressure have little or no dyspnea it is probable that such chronic cases accommodate themselves more or less to the high venous pressure increased blood carbon dioxide and decreased blood oxygen in contrast to the dyspneic reaction of acutely congested cases Moreover it is of interest to observe occasionally *the disappearance of dyspnea (due to left ventricular failure)* when the right ventricle fails secondarily and no longer maintains the congestion of the lung vessels

Orthopnea (ορθο erect and πνοη breathing) is the term applied to dyspnea sufficient in degree to force the patient to assume a sitting position such a position acts by gravity to relieve some of the congestion in lungs and brain

2 *Cardiac asthma* (ασθμα gasping) When congestion of the pulmonary circulation occurs suddenly as the result either of acute failure of the left ventricle (see Chapter 30) or of tachycardia in cases of marked mitral stenosis (see Chapter 26) the tension or emphysema (εμ into and φυσημα a blowing sound) that ensues may by nervous reflex action precipitate asthmatic breathing this is cardiac asthma it is not adequately described by any other term such as paroxysmal dyspnea or acute pulmonary edema Of course there is always dyspnea in such cases but asthmatic respiration is a particular type of dyspnea moreover there may or may not be clinically so-called frank pulmonary edema in these cases that is the blood vessels may be greatly engorged with or without interstitial edema but with no actual fluid in the alveoli and bronchioles In fact the squeaking rales of pulmonary emphysema and asthma are much more common in these patients than are moist rales

An attack of cardiac asthma most commonly comes suddenly at night when a patient with chronic heart disease is sound asleep with head and thorax low in position It may infrequently occur on unusual effort when awake The kind of heart disease is that causing severe strain on the left ventricle, especially hypertension aortic stenosis or regurgitation or coronary thrombosis except in rare cases of marked mitral stenosis when tachycardia due to exercise or excitement or occurring paroxysmally suddenly floods the pulmonary circulation

It is important to note that pulmonary congestion or edema may occur acutely or chronically without asthma that asthmatic breathing occurs often without any heart disease at all, but that in an asthmatic type' of individual cardiac asthma is precipitated by acute congestion of the pulmonary circulation it is as Hope pointed out over one hundred years ago (1832), merely bronchial asthma due to bronchiolar spasm added to and set off by heart

failure (see Chapter 30) Cardiac asthma like bronchial asthma is helped though less dramatically by theophylline ethylene diamine (aminophyllin) administered intravenously

3 *Periodic apnea and hyperpnea* (*Cheyne Stokes respiration*) is not pathognomonic of heart disease but it occurs most frequently in chronic cardiac cases with left ventricular weakness combined with an especially poor blood supply to the respiratory center It comes on at first commonly during sleeping hours and tends to begin in very slight degree that is with waxing and waning of respiration but not actually apnea and hyperpnea it is not then such an important sign but its progress should be watched for when it is present during the waking hours it is a serious prognostic sign It is the result of alternating overstimulation of the respiratory center by blood oxygen lack and carbon dioxide excess and overdepression by blood oxygen excess and carbon dioxide decrease It is best treated by stimulation of the respiratory center by theophylline ethylene diamine (aminophyllin) or caffeine along with routine treatment of the myocardial weakness (see Chapter 30)

Palpitation (from the Latin *palpitare* to throb) Palpitation is a much less important heart symptom than pain and dyspnea It consists of an unpleasant sensation of the heart s action whether slow or fast regular or irregular It is usually the result of unimportant disturbance of heart rhythm namely premature beats or extrasystoles and paroxysmal tachycardia (see Chapter 32) or of forceful regular heart action rapid or slow the result of effort excitement toxic effect (for example from tobacco) or infection in a nervously sensitive person Infrequently it may be caused by a more important disorder of heart rhythm such as atrial fibrillation atrial flutter or heart block (see Chapters 33 and 34) In addition to the sensation of palpitation in the thorax there is frequently a sensation of pulse throbbing in the head or extremities more often in the arms than in the legs This is usually regular and forceful and due to effort excitement nervousness fever thyrotoxicosis or reaction to various substances ingested or inhaled for example alcoholic drinks tobacco nitrites It is not per se a sign of heart disease though it is increased in the presence of aortic regurgitation or other cause of a full pulse pressure If present in an observer it may sometimes be difficult to distinguish between his own pulse and the pulse of the subject being examined except by rate

Other symptoms There are several other symptoms frequently occasionally or rarely associated with heart disease but not often directly related Exhaustion nervousness insomnia dizziness headache cough hoarseness hemoptysis faintness syncope anorexia and pain in abdomen or legs are usually but incidental to various complications of heart disease examples are periodic pain in the legs on walking due to arteriosclerosis and faulty blood supply to the muscles (intermittent claudication) and nervousness due to neurocirculatory asthenia Dizziness faintness and even circulatory collapse are sometimes wrongly accredited to heart disease (for example acute coronary occlusion) when actually a severe grade of Meniere s syndrome is present with

faulty function of the internal ear the clue rests in the presence of marked *vertigo* (with nausea as a rule) which is not a symptom of heart disease although mild grades of Meniere's syndrome are frequent accompaniments of hypertension and the degenerative types of heart disease in older persons

Several noncardiac symptoms are at times directly related to heart disease Insomnia may be the result of a poorly defined orthopnea secondary to left ventricular failure and pulmonary vascular congestion Anorexia and upper abdominal pain may be due to engorgement of liver stomach and intestines secondary to right ventricular failure Syncope (with or without convulsions) may be the result or prolonged cerebral anemia secondary to ventricular stand still in heart block of high degree or to extreme tachycardia in paroxysms and rarely a manifestation of angina pectoris a sensitive carotid sinus reflex or a vasovagal reflex of other cause Cough dry in character and sometimes metallic or brassy in quality may result from pressure on air passages or recurrent laryngeal nerve through the presence of aortic aneurysms very large hearts or massive pericardial effusions irritation of pleura or of diaphragm in acute pericarditis may also occasion cough Both cough and hemoptysis may be due to pulmonary vascular congestion in cases of left ventricular failure and of mitral stenosis Hoarseness may appear in rare *cases of aortic aneurysms and mitral stenosis Dysphagia may be caused by* a saccular or dissecting aortic aneurysm anomalous aortic arch dilated left atrium or a large pericardial effusion

BIBLIOGRAPHY

THE PATIENT'S HISTORY SYMPTOMS

SEE ALSO GENERAL REFERENCES FOLLOWING CHAPTER 2

Adams R Cases of Diseases of the Heart Accompanied with Pathological Observations *Dublin Hosp Rep* 1827 IV 353

Bloomfield A L Dysphagia with Disorders of Heart and Great Vessels *A J M Sc* 1940 CC 289

Boyer N H and White P D Right Upper Quadrant Pain on Effort An Early Symptom of Failure of the Right Ventricle *New England J Med* 194. CCXXVI 217

Capps J A Pericardial Pain An Experimental and Clinical Study *Arch Int Med* 1927 XL 715

Capps J A and Coleman G H *An Experimental and Clinical Study of Pain in the Pleura Pericardium and Peritoneum* Macmillan Co New York 1932

Capps R B "Cause of So-Called Side Ache that Occurs in Normal Persons Personal Observations *Arch Int Med* 1941 LXVIII 94

Cheyne J "A Case of Apoplexy in which the Fleshy Part of the Heart was Converted into Fat *Dublin Hosp Rep* 1818 II 216

Currens J H and White P D "Cough as a Symptom of Cardiovascular Disease *Ann Int Med* 1949 XXX 528

Hamman L Spontaneous Mediastinal Emphysema of the Lungs *Tr A Am Physicians* 1937 LII 311 and *Bull Johns Hopkins Hosp* 1939 LXIV 1

Harrison T R Calhoun J A Cullen G E Wilkins W E and Pilcher C Studies in Congestive Heart Failure XV Reflex versus Chemical Factors in the Production of Rapid Breathing *J Clin Investigation* 1932 XI 133

Hope J *A Treatise on the Diseases of the Heart and Great Vessels* William Kidd London 1832 p 205

Kellogg F and White P D "The Clinical Significance of Precordial Tenderness—The Relationship of Such Tenderness to Pain" *New England J Med* 1932 CCVI 659

Lewis T *Pain* Macmillan Co New York 1942

McGinn S and White P D "A Follow up Report on the Clinical Study of Two Hundred and Fifty Cases of Cardiac Asthma and a Survey of an Additional Group of Twenty two New Cases *New England J Med* 1932 CCVII 1069

Acute Pulmonary Congestion and Cardiac Asthma in Patients with Mitral Stenosis" *Am Heart J* 1934 IX 697

Mackenzie J The Nature and Significance of Heart Symptoms *Brit M J* 19_2 I 505

Palmer R S and White P D "The Clinical Significance of Cardiac Asthma Review of Two Hundred and Fifty Cases *J A M A* 1929 XCII 431

Sprague H B Heart Attacks" *Boston M and S J* 1927 CXCVI 472

Stokes W Observations on Some Cases of Permanently Slow Pulse *Dublin Quart J* 1846 II 73

"On Fatty Degeneration of the Heart Chapter V of *The Diseases of the Heart and the Aorta* Hodges and Smith Dublin 1st ed 1854

White J C and Smithwick R H *The Autonomic Nervous System Anatomy Physiology and Surgical Treatment* Macmillan Co New York 2nd ed 1941 (1st ed 1935)

White P D and Hahn R G "The Symptom of Sighing in Cardiovascular Diagnosis with Spirographic Observations" *Am J M Sc* 1929 CLXXVII 179

CHAPTER 4

PHYSICAL EXAMINATION

SIGNS WITH ESPECIAL REFERENCE TO CYANOSIS JAUNDICE AND EDEMA

Having obtained the fullest possible information from the patient s own history the physician turns next to the physical examination which fills most of the gaps left in the completion of the picture of the condition of the heart In the writer s experience the relative values of the different parts of the examination are about as follows in percentage of the total history 45 per cent physical examination 25 per cent electrocardiography 15 per cent roentgenology 10 per cent other methods of examination (blood urine basal metabolic rate cardiac catheterization circulation rate vital capacity and functional tests) 5 per cent

There was somewhat of a danger of overemphasis of symptoms and *of tests* of reserve in the years that followed World War I to the neglect of physical signs This situation was the result of two factors in the first place for ten years or more before that war the pendulum had been set swinging from the *extreme point of view of the nineteenth century that structural* defects and evidence thereof should be the focus of medical diagnosis prognosis and treatment to the opposite extreme of prime consideration of the functional state of the circulation and secondly the need of manpower for the armed forces during that war forced disregard for ultimate in favor of immediate prognosis The situation was more favorable in this respect so far as the U S A was concerned in World War II

Clues to the etiology of heart disease and to the functional state of the circulation are frequently found in signs other than those presented by the heart directly It is therefore essential in the physical examination of an *individual* suspected of having trouble with the heart to search the whole body for such clues Hence before taking up the examination of the heart itself I shall present the more important signs of heart trouble elsewhere in the body and discuss in somewhat more *detail three special conditions—cyanosis* jaundice and edema

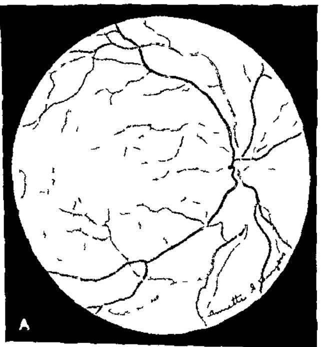
In the first place the general appearance of the patient is of vital importance

this includes age build height and weight (and especially their relationship) nutrition strength mental state color and breathing These various points are often taken in at a glance without careful analysis but they weigh heavily in the final assessment of the case thus affording the physician who personally examines the patient a great advantage over the doctor who is asked to make his diagnosis and prescribe treatment on the basis of hearsay evidence only no matter how careful and detailed may be the history and report of physical signs

Head and neck The eyes afford more clues in a cardiac patient than any other part of the body except the neck and the heart itself Exophthalmos and related eye signs suggest at once the probability that at least some of the heart trouble is due to thyrotoxicosis The failure of the pupils to react to light (Argyll Robertson pupil) and their irregularity and inequality indicate at once the need to search for aortitis itself since central nervous system syphilis and cardiovascular syphilis are frequently associated The arcus senilis is not an important clue however it is only a little more common in older individuals with heart disease than in those without The same statement is true of cataracts The eye grounds on the other hand are of considerable importance especially when there is uncertainty about the degree the duration or even the past existence of high blood pressure important hypertension is attended in the course of a few years by sclerosis of the small arteries of the eye grounds which becomes marked in degree and may be attended by edema exudate hemorrhages and even choking of the disks, when the hypertension becomes malignant (Figure 9) Petechial hemorrhages in the conjunctivae are frequently found in subacute bacterial endocarditis

The mouth and throat should be examined for infection of teeth gums and tonsils which may sometimes lead to acute rheumatic heart disease or to acute or subacute bacterial endocarditis in persons susceptible to these diseases (see Chapters 14 and 15)

The neck may show several important abnormalities Thyroid gland enlargement suggests thyrotoxicosis Vigorous arterial pulsation with the subject at rest is indicative of chronic hypertension aortic regurgitation or aneurysmal dilatation A tracheal tug (sometimes called Oliver s sign Oliver 1878) is uncommon when it is clearly evident it points to the presence of an aortic aneurysm Increased activity of the carotid sinus reflex determined by firm pressure exerted by the fingers high up on the carotid artery in the region of the bulb may reveal itself in marked slowing of the heart rate drop in blood pressure or reflex cerebral vasoconstriction with resulting faintness or syncope such a finding may be helpful in explaining symptoms of obscure origin (Weiss and Baker 1933) Finally and most important of all there is engorgement or pulsation of the jugular veins with the subject in the upright position this means most commonly congestive heart failure involving the right ventricle or the whole heart less often it means acute or chronic constrictive pericarditis which blocks the entrance of blood into the heart and least often it indicates organic tricuspid stenosis or regurgitation or obstruc-



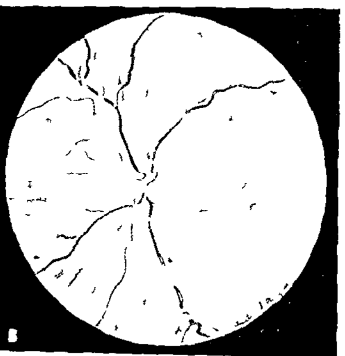


FIG 9 *Photographs of the fundus oculi* (*A*) Right eye of a normal blond man age 23 (*B*) Left eye of a 36 year old blond man with malignant hypertension retinal arteriosclerosis and generalized arteriosclerosis Blood pressure 240 mm mercury systolic and 142 *mm diastolic* Albuminuria and granular casts Retinal arteries tortuous irregular in caliber and in various stages of sclerosis Veins are engorged irregularly dilated and markedly compressed by superimposed arteries The superior temporal vein is bordered by white lines *Light streaks* are increased on the arteries and on the anterior arches of the veins The relatively normal fovea with its reflex resembles the so-called "hole in the macula owing to surrounding retinal edema Scattered over the fundus there are two kinds of exudates *one pale yellowish white solid looking the other (around macula)* small superficial white line powdered snow Radiating from the disk in the manner of opaque nerve fibers there are areas of retinal edema stretching into the periphery and in spots obscuring the blood vessels There are many small retinal hemorrhages in various stages of absorption Th e wa a n la cond t on n the ght eye (Kindness of Mrs W ll m H W lm B lt m e)

tion of the superior vena cava by tumor aneurysm or other mediastinal in volvement The deep systolic jugular pulse should not be confused with the carotid pulse (see Chapter 8)

Thorax Chest deformities have two interesting relationships to heart disease Precordial bulging of the bony thorax without other important de formities signifies usually the development of cardiac enlargement due to con genital defects or rheumatic involvement during the period of early growth it is therefore valuable as a sign of important affection of the heart in early childhood Marked scoliosis and kyphosis may themselves give rise to heart disease or more often to insufficiency of the lungs and in rare cases a de pressed sternum may embarrass the heart (see Chapter 23) Abnormal pulsa tions and elevations of the chest wall are found in cases of aortic aneurysm (Figure 10) and of cardiac hypertrophy Palpation of the intercostal spaces



FIG 10 Photograph showing a localized bulging at the right of the upper sternum due to an aneurysm of the ascending aorta and innominate artery

in the dorsal and axillary parts of the thorax may reveal arterial pulsations that indicate the presence of congenital coarctation of the aorta Cardiac pulsations will be discussed in the next chapter

Examination of the lungs is of great importance in heart disease There may be moist rales at the bases due to pulmonary edema resulting from failure of the left ventricle but such rales must be carefully distinguished from atelectatic rales and from rales due to pulmonary infection or multiple infarction distinctions which are frequently neglected Moreover too much has been made of this sign in contrast to that of simple dyspnea or of emphysema with wheezy respiration due to the more common engorgement of the pulmonary circulation in failure of the left ventricle and in mitral stenosis of high degree The emphysema in such cases is primarily a functional state and not usually discoverable at postmortem examination when the lung vessels are emptied it is due to the stiffening of the lung fixation of the alveoli and low position of the diaphragm with the result that relatively little air passes in and out and that only with considerable difficulty Areas of pulmonary consolidation are quite common in heart disease especially infarcts complicating congestive heart failure or mitral stenosis These infarcts are due to embolism from venous thrombosis in abdomen pelvis or legs (most commonly saphenous and femoral venous thrombosis) resulting from the slowed circulation with or without actual phlebitis and are often serious occasionally terminal and frequently overlooked or wrongly labeled pneumonia much less commonly such embolism originates from the right heart chambers Other consolidation of lung tissue may complicate heart disease especially hemorrhagic involvement in severe active rheumatic infection and occasionally a real pneumonic process Finally signs of hydrothorax in a cardiac patient are common the result of an active rheumatic pleuritis or a part of a polyserositis which is usually of unknown etiology or most frequently a transudate due to congestive failure of the right ventricle or whole heart involving especially the right side of the thorax Right hydrothorax is more frequent than left either because of the greater ease of obstruction of the azygos vein on that side or else because of higher venous pressure in the pulmonary circulation of the right lung than in that of the left lung in congestive heart failure (Dock, 1935, White August and Michie 1947) Ewart s sign (Ewart, 1896 Levine and Gevalt, and Gordon 1940), consisting of dullness, increased fremitus and bronchial breathing at the left lung base in cases of pericardial effusion is probably the result of several factors including compression of the lung by fluid in the pleural as well as in the pericardial cavity and pulmonary infarction

Interstitial emphysema of the mediastinum (with or without pneumothorax) is revealed by curious crackling sounds heard over the sternum and sometimes by palpable subcutaneous emphysema in neck or over the anterior thoracic wall (Hamman, 1939 Griffin 1942)

Abdomen There are three signs obtained by examination of the abdomen that are of significance in a cardiac patient The first is enlargement of the liver from engorgement due to congestive failure of the right ventricle to tri

cuspid stenosis or to acute or chronic constrictive pericarditis If the congestion occurs quickly the liver is tender because of the rapid stretching of its capsule Pulsation of the liver that is easily discernible is rare it is the result either of advanced congestive failure of the right ventricle with functional tricuspid regurgitation as in mitral stenosis of long standing or of tricuspid valve disease (rheumatic) of high degree Cirrhosis of the liver may be a coincidental complication of heart disease and failure but in lesser degree it may be a sequel of chronic constrictive pericarditis or mitral stenosis of long standing The second important abdominal sign in heart disease is splenomegaly which is confirmatory of the diagnosis of subacute bacterial endocarditis The third sign is ascites (ασκος bag or bladder) which in a cardiac patient is usually the result of congestive failure of the right ventricle but which may also be caused by tricuspid stenosis or chronic constrictive pericarditis in both of which conditions it more or less parallels the degree of liver engorgement ascites may also be a part of a polyserositis (Concato s disease) which forms the background for chronic constrictive pericarditis (Pick s disease) and it may likewise be caused or aggravated by a complicating cirrhosis of the liver When the possibility of syphilitic aortitis exists inspection of the genitalia for the scar of a chancre may prove helpful

Extremities Abnormal pulses dependent edema cyanosis clubbing of the fingers and toes polyarticular rheumatism and rheumatic nodules are the special signs to be looked for here in a cardiac patient The pulse will be discussed in Chapter 8 Clubbing of fingers and toes associated with cyanosis is found in certain congenital cardiovascular defects (the morbus caeruleus) (see Figure 63 page 298) Clubbing without cyanosis is found in subacute bacterial endocarditis However it must be remembered that clubbed fingers are often found with noncardiac conditions most commonly of all in pulmonary diseases even ulcerative colitis may be the underlying cause and a familial type of unknown etiology has been described Recently it has been found that in all varieties of simple clubbing except hereditary the blood flows per unit surface or volume of finger tip are abnormally high as the result of reduction of the brachial-digital blood pressure gradients this increase of blood flow is probably the important factor in the development of the clubbing (Mendlowitz 1941)

Rheumatic nodules are important evidence of an active rheumatic infection but must be differentiated from the nodes of rheumatoid arthritis (see Figure 84 page 367) It is well also to palpate the dorsalis pedis and posterior tibial arterial pulses if they are much diminished or absent we have evidence as a rule of arteriosclerosis of high degree which may not be limited to the legs or in rare cases of congenital coarctation or of dissecting aneurysm of the aorta Finally absence of the knee jerks suggests the need of searching carefully for syphilitic aortitis while their exaggeration points to the presence of a hypersensitive nervous system which may accentuate cardiac symptoms As a rule the more lively both knee jerks the less serious are the symptoms

There are three particular signs in a cardiac patient that deserve consideration at some length they are cyanosis jaundice and edema

Cyanosis Cyanosis (κυανος dark blue color) of skin and mucous membranes is a sign much sought for but unless the cyanosis is well marked or constant it may be unimportant since it often results from temporary local disturbances of the circulation and not from serious disease of heart lungs or blood vessels This change in color is the result of the presence in dilated superficial blood vessels of venous blood in which an abnormally high percentage of the hemoglobin has lost its oxygen (reduced hemoglobin) Two factors are of much importance in determining the degree of cyanosis first the extent of oxygen dissociation or reduction of hemoglobin and second, the degree of dilatation of the blood vessels (arterioles and capillaries) of the skin and mucous membranes which makes the cyanosis visible The less the oxygen saturation of the hemoglobin and the more dilated the superficial vessels the greater is the degree of cyanosis in any part of the body Arterial blood should normally be 95 to 100 per cent saturated with oxygen which is equivalent to 19 to 20 volumes per cent (the normal oxygen content of atmospheric air) if it is but 80 to 85 per cent saturated so that it contains 3 or 4 volumes per cent of reduced hemoglobin cyanosis results The capillary blood should normally contain about 3 5 volumes per cent of reduced hemoglobin if it contains over 6 5 volumes per cent there results a cyanotic color like that of venous blood which normally contains about 6 volumes per cent of reduced hemoglobin As a rule cyanosis is most common and best seen in lips cheeks ears and hands where the blood vessels are numerous and most exposed to the air This condition is sometimes called *acrocyanosis* (ακρος outermost and κυανος cyanosis) A further factor in the production of cyanosis is the amount of hemoglobin in the blood with an increased amount as in polycythemia the blood possesses a much more pronounced blueness of color due to the high total content of reduced hemoglobin than when there is dilution as in anemia even though the percentage of reduction of the hemoglobin is the same

The underlying causes of cyanosis are seven

1 The first and most common factor is local and consists of the slowing of the peripheral circulation by cold or vasomotor nervous stimulation Arteriolar vasoconstriction reduces the capillary blood pressure and speed of flow This slowed circulation of the blood allows a greater dissociation of oxygen than usual hence the cyanosis If the cold becomes intense however the dissociation of oxygen stops and even though the circulation remains very slow the skin color is red and not blue due to the presence of arterial blood An abnormally high degree of sensitiveness to cold especially in the hands with the paroxysmal production of cyanosis (or pallor) is seen in the condition called Raynaud s disease (see Chapter 31) The high degree of circulatory disturbance in this condition is usually attended by pain Probably both cold and vasomotor nervous stimulation act together in Raynaud s disease

2 Obstruction to the return of blood to the heart may also cause cyanosis either from internal cause namely congestive failure of the right ventricle tricuspid stenosis or acute or chronic constrictive pericarditis or from local causes namely pressure on the veins by tumor or constriction venous thrombosis or incompetent venous valves The slowing of the blood flow through the vessels of the skin causes increased dissociation of oxygen and a blue color exaggerated by capillary dilatation

3 A third very important factor is congestion of the lungs due to heart trouble A chronic engorgement of the lung vessels in mitral stenosis or acute or chronic engorgement from failure of the left ventricle causes a certain amount of blood to pass through the lungs in the middle of the dilated capillaries and so out of contact with the alveolar air continuing into the systemic circulation as venous or blue blood with a considerable dissociation of oxygen If enough of the blood one third it has been estimated is so shunted from venous system to arterial system cyanosis will result Often combined with this factor of engorgement of the lung vessels is that of slowing of the return of blood to the heart from various causes Thus one factor may reinforce another in the production of cyanosis

4 Certain congenital heart defects may cause cyanosis by shunting venous blood directly into the systemic circulation via a single ventricle or dextroposed aorta overriding both ventricles or in transposition of the great vessels or less commonly and later in life through interventricular or interatrial septal defects or patent ductus arteriosus It has been calculated that 30 to 40 per cent of the venous blood must be so shunted in order to assure the presence of cyanosis In patients of this type the capillaries of the skin have been found dilated and the peripheral circulation slowed and it has been suggested that this local factor may be more important in the production of cyanosis than the congenital heart disease itself It is likely however that the veno arterial shunt alone is responsible for most of the cyanosis which is in turn deepened or perhaps even brought to notice by the slowing of the peripheral circulation the slowing of the peripheral circulation is occasioned by the need of the tissues to remove sufficient oxygen from the oxygen deficient blood stream The polycythemia present in most cases of congenital heart disease with a right to left shunt is an additional factor which exaggerates cyanosis Congenital heart defects in which there is no veno arterial shunt are not attended by cyanosis unless there is a complicating factor of congestive heart failure or pulmonary disease

5 Disease of the lungs acute or chronic may be a cause of cyanosis the presence and degree of which are dependent on the amount of pulmonary involvement and on the presence of complicating factors With consolidation of much lung tissue in pneumonia or infarction venous blood in sufficient amount to cause cyanosis is shunted through the pulmonary circulation without coming into contact with alveolar air Moisture in the alveoli and bronchioles may act even more than consolidation to cause cyanosis by preventing contact of blood with air as is the case with severe influenza or

inversely but not in the same degree In nephrosis and starvation edematous fluid is very low in protein giving percentages lower than in any other conditions while the fluid from lymphedema and also from edema in inflammatory areas has a high content of protein the more purulent the inflammatory edema is the higher its protein content and the nearer it approaches the chemical state of blood serum The specific gravity of edematous fluids varies with the protein content *from about 1 008 with very little protein to 1 020 or more* approaching the specific gravity of blood serum itself Ascitic and hydrothoracic fluids or so called transudates in congestive heart failure have the same composition as subcutaneous edema fluid except for a somewhat higher protein content and a higher specific gravity (about 1 012)

Most of the underlying causes of edema are known In the first place there is the simple effect of gravity Standing long in one position with little or no movement of the legs (contraction of the leg muscles favors an upward flow in the veins) causes a slowing of the circulation with increase in size of the legs from stasis progressing in extreme cases to actual edema which is usually most evident in the ankles just above the shoes and over the shins This edema becomes palpable it is said when the limb volume has increased by 8 per cent The heavier the person and the longer the time on the feet the more likely is the appearance of edema This edema may be regarded as a physiologic occurrence when it is found in heavy persons who stand much of the time Walking or other movement of the feet and legs aids the circulation and tends to prevent edema The presence of varicose veins favors its occurrence especially unilaterally or preponderantly in one leg or the other

Besides gravity a common cause of edema and one of the most frequent is obstruction to the return flow of fluid from tissues to heart Lymphatic block is rarely the cause of any important edema although it may in exceptional cases give rise to chronic massive increase in size of legs or arms or genitalia called elephantiasis Obstruction of the venous circulation is frequently responsible for edema This obstruction may come in a variety of ways (1) by venous thrombosis due to inflammation or to stasis (2) by *pressure on veins from without* by tumors scars and tight bands and more or less normally late in pregnancy (in the last four weeks) and (3) by resistance to the flow of blood into the heart usually because of the inability of the right ventricle from failure or otherwise to pass on all the blood it receives This venous obstruction also may be due to tricuspid stenosis or to limitation of the size of right heart chambers and venae cavae by a large pericardial effusion or by chronic constrictive pericardial adhesions (as in Pick s disease) so that too small an amount of venous blood enters the heart in diastole with resulting accumulation of edema fluid in tissues and serous cavities The explanation of edema secondary to obstruction of the return flow of blood to the heart from any cause is the increased hydrostatic pressure in the venous ends of the capillaries which results from the increased pressure in the systemic veins and which prevents the normal absorption of fluid from *the tissues* Krogh Landis and Turner (1932) demonstrated that excessive

fluid accumulates in the tissue spaces in man when the venous pressure (normally 6 to 8 cm of water) is raised above 15 to 20 cm

Another important type of edema but much less common than that resulting from venous obstruction with or without cardiac cause is that dependent on physiochemical factors which produce a disturbance of the normal osmotic pressure relationship between the fluids in capillaries and tissues Here disorders of either liver or kidneys may play an important role with the onset of a spontaneous diuresis heralding a beginning recovery The higher concentration of substances in particular proteins which diffuse with difficulty through the capillary wall in the blood stream than in the body tissues establishes an osmotic pressure which normally draws fluid from tissues into the blood and so tends to neutralize the hydrostatic pressure so far as the fluid balance on both sides of the capillary walls is concerned Nephritis especially with nephrosis and disturbances of tissue metabolism due to starvation are frequently associated with edema this edema is usually general in distribution affecting face arms and hands and not simply the dependent portions of the body as in congestive heart failure Nephritic edema is due fundamentally to damage to the renal tubules which prevents the concentration of the urine and the reabsorption of albumin the low content of albumin in the capillary blood serum prevents the proper return flow of fluid by osmotic pressure into the blood from the tissues A certain type of nephritis with free loss or leakage of sodium tends like Addison s disease with its faulty sodium metabolism toward dehydration and collapse and not edema

Edema secondary to decreased negative osmotic pressure of the blood may be added to edema due to increased positive hydrostatic capillary pressure in a patient with congestive heart failure and malnutrition this is a point of much importance and explains obscure findings in some cases The excessive ingestion of sodium chloride particularly in cases of low myocardial reserve also favors the accumulation of edema in the body tissues

Another important cause of edema in congestive heart failure seems to be due to deficient circulation to the kidneys secondary to failure of the myocardium of the left ventricle or of the whole heart and resulting in inability of the kidneys to excrete sodium normally the retention of sodium results in the building up of the body water both in and out of the circulation

Recently Sarnoff (personal communication 1951) has found that in experimental animals excessive stimulation of the vasomotor center in the brain can result in such peripheral vasoconstriction that blood is rapidly transferred in bulk from the systemic circulation to the pulmonary circulation resulting in pulmonary edema this is probably an explanation for the so-called neurogenic or cerebral type of pulmonary edema

The metabolic disorder of hypothyroidism (myxedema) is commonly associated with a nonpitting accumulation of fluid in the body tissues generally (not primarily in dependent parts of the body) and is attended by a low blood plasma volume in contrast to cardiac edema thyroid therapy clears this myxedema

Beriberi (avitaminosis) is attended by the accumulation of fluid in body tissues but rarely by frank edema

A rare type of edema of unknown cause is hereditary in nature (Milroy 1892 Braham and Howells, 1948)

There are two other varieties of edema that need little comment here because of their ease of recognition and their absence of connection with cardiovascular disease (1) local tissue edema associated with an infectious or toxic process the commonest kind of edema of all and (2) angioneurotic edema (Quincke 1882) also generally localized

Edema due to heart disease may be of any degree from slight edema of the lungs or over ankles or shins developing after a considerable length of time in the standing position to massive edema (called *anasarca* ανα upon or throughout and σαρξ flesh) of much of the body in extreme cases even affecting the arms chest wall and face With extensive cardiac edema fluid tends to accumulate also in the peritoneal cavity (ascites) pleural cavities (hydrothorax) especially the right where it appears earlier than in the left and even in the pericardium (hydropericardium) Edema of one side of the body (as of face arm chest abdominal wall or leg) may sometimes be more marked than that of the other side it may be found that this is the effect of gravity the patient having been lying on that side of the body When however in an ambulatory patient edema is confined to one leg or is much more marked in one leg than in the other local venous obstruction (or vasodilatation) is the probable cause Cardiac edema may be associated with some other type of edema in the same case

Edema of the brain is the result of infection hemorrhage infarction or toxic influences such as alcoholism its occurrence in heart disease is not clearly recognized even when there is extensive anasarca involving the upper part of the body in the course of extensive congestive heart failure Edema of lungs may be found in noncardiac patients as the result of infection infarction nephritis or toxic state or as an unusual reflex to pleural trauma or to central nervous system disease when of cardiac origin it results from failure of the left ventricle or from obstruction to the entrance of blood into the left ventricle by marked stenosis of the mitral valve It is to be noted that pulmonary edema is due to left ventricular failure and not to right ventricular failure in fact when right ventricular failure follows failure of the left ventricle as often happens, congestion and edema of the lungs decrease and sometimes disappear entirely Edema of the liver and other abdominal and pelvic viscera is commonly due to failure of the right ventricle or of the whole heart to marked tricuspid stenosis or to acute or chronic constrictive pericarditis Edema of heart and skeletal muscle is not common it has been noted in extensive general anasarca and in beriberi

Finally it is to be noted that bilateral pitting edema of the legs is much less commonly due to heart failure than to other causes especially local venous circulatory fault even in cardiac patients themselves Much digitalis has been wastefully prescribed in such cases before careful appraisal of the heart itself

has demonstrated its futility in these patients of course heart failure may by chance eventually supervene and then digitalis may clear the new increment of edema

BIBLIOGRAPHY

SIGNS WITH ESPECIAL REFERENCE TO CYANOSIS JAUNDICE AND EDEMA
SEE ALSO GENERAL REFERENCES AFTER CHAPTER 2

Braham J and Howells G Hereditary Oedema (Milroy s Disease) *Brit M J* 1948 I 830

Dock W 'The Anatomical and Hydrostatic Basis of Orthopnea and of Right Hydro thorax in Cardiac Failure *Am Heart J* 1935 X 1047

Drinker C K Field M E and Homans J Experimental Production of Edema and Elephantiasis as a Result of Lymphatic Obstruction *Am J Physiol* 1934 CVIII 509

Elias H and Feller A *Stauungstypen bei Kreislaufstorungen Mit besonderer Beruck sichtigung der exsudativen Perikarditis Eine anatomische experimentalle und klinische Untersuchung* Julius Springer Vienna and Berlin 1926

Ewart, W Practical Aids in the Diagnosis of Pericardial Effusion *Brit M J* 1896 I 717

Foote S A Jr Reed W C Comeau W J and White P D The Clinical Significance of Bilateral Edema of the Lower Extremities *Am J M Sc* 1940 CXCIX 512

Griffin R J "A Diagnostic Sign of Spontaneous Interstitial Emphysema of the Mediastinum *Ann Int Med* 1942 XVII 295

Hamman L Spontaneous Mediastinal Emphysema *Bull Johns Hopkins Hosp* 1939 LXIV 1

Keefer C S and Resnik W H Jaundice Following Pulmonary Infarction in Patients with Myocardial Insufficiency I A Clinical Study *J Clin Investigation* 1926 II 375 II An Experimental Study *Ibid* p 389

Krogh A Landis E M and Turner A H The Movement of Fluid Through the Human Capillary Wall in Relation to Venous Pressure and to the Colloid Osmotic Pressure of the Blood *J Clin Investigation* 1932 XI 63

Levine S A and Gevalt F C Jr with discussion by Gordon A H The Significance of Ewart s Sign *Tr A Am Physicians* 1940 LV 106

Lundsgaard C and Van Slyke D D Cyanosis " *Medicine Monographs* Williams and Wilkins Co Baltimore 1923

Meakins J The Distribution of Jaundice in Circulatory Failure " *J Clin Investigation* 1927 IV 135

Mendlowitz M Measurements of Blood Flow and Blood Pressure in Clubbed Fingers *J Clin Investigation* 1941 XX 113

Milroy W F An Undescribed Variety of Hereditary Oedema " *New York M J* 1892 LVI 505

Oliver W S "Physical Diagnosis of Thoracic Aneurysm *Lancet* 1878 II 406

Quincke H I Uber akutes umschriebenes Hautodem *Monatsch f prakt Dermat* 1882 I 129

Sarnoff S J Massive Pulmonary Edema of Central Nervous System Origin Hemo dynamic Observations and the Role of Sympathetic Pathways *Federation Proc Fed Am Soc of Exper Biol* 1951 X 118

Stead E A Jr Edema of Heart Failure *Bull New York Acad Med* 1948 XXIV 607

Weiss S and Baker J P Carotid Sinus Reflex in Health and Disease Its Role in Causation of Fainting and Convulsions *Medicine* 1933 XII 297

White P D August S and Michie C R Hydrothorax in Congestive Heart Failure *Am J M Sc* 1947 CCXIV 243

Youmans J B Bell A Donley D and Frank H Endemic Nutritional Edema I Clinical Findings and Dietary Studies *Arch Int Med* 1932 L 843

CHAPTER 5

PHYSICAL EXAMINATION OF THE HEART ITSELF

INSPECTION PALPATION PERCUSSION AND AUSCULTATION

This chapter and the next along with Chapters 3 and 4 concern themselves with the simplest and yet the most fruitful methods of examination requiring only the use of the voice the ears the eyes the fingers the stethoscope the blood pressure instrument and especially the intelligence all of which are at once available to the practicing physician Time and effort supply the necessary experience

One is very prone in these days of the machine age to abandon the patient training and skilled use of the unaided senses Nowhere is this truer than in the practice of medicine It has become rather too easy in hospitals or even in the doctor s office to make a roentgen ray examination of the heart and to neglect inspection palpation and percussion But the senses of sight touch *and hearing unaided by instruments except for the simple convenience* of a stethoscope and of a sphygmomanometer are still well worth cultivating When the senses are highly trained and skillfully used they establish such a justified feeling of confidence that it is possible to obtain much information about heart size and shape even when the roentgen ray is not available and also to secure other important data about the heart not shown by the roentgen ray *as in the case of palpable thrills and changes in heart sounds and the presence* of murmurs which reveal much concerning the structural changes in the heart and its functional condition

INSPECTION AND PALPATION

The first important thing to attempt to do on examination of the heart is to locate *the position of the apex* best done with the subject seated and the thorax inclined slightly forward This is possible in the great majority of cases failing only in a few obese or very sick patients Both inspection and palpation aid in this purpose but more especially palpation which by the use of the trained fingers permits the identification of the maximal impulse as the site *of the cardiac apex Such identification is usually in agreement* within a few

millimeters with the position of the apex as determined by orthodiagraphy A measurement of the horizontal distance of the maximal apex impulse from the midsternal line tangentially to the front of the chest is recorded in centimeters and compared to the position of the midclavicular line which is a vertical line dropped from a point halfway between the midsternum and the outer end of the left clavicle as noted below (Figure 11) The position of the cardiac apex should lie in the left fifth intercostal space in or to the

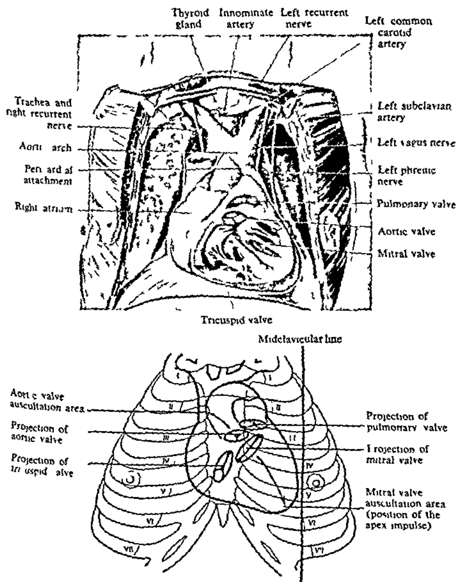


FIG 11 Topographic relationships of the heart and great vessels The heart chambers and blood vessels are shown in a distended state (Corning *Lehrbuch der topographischen Anatomie* 1917)

right of the midclavicular line in a normal adult sitting or standing except in rare instances when the heart may be displaced upward and a little outward from great abdominal distention as in pregnancy The average position of the midclavicular line in the normal adult is 8 to 8½ cm to the left of the midsternum varying from 7 to 10 in the extremes of body size The maximal apex impulse falls normally on this line or ½ to 1 cm within it rarely when the thorax is long and the heart vertical in position so that it is almost centrally placed in the chest the cardiac apex is low often behind the sixth rib or rarely in the sixth intercostal space and as much as 1½ to 2 cm medial to the midclavicular line If it is beyond the midclavicular line in the fifth space enlargement of the heart is to be diagnosed unless the heart is displaced by fluid or air in the right pleural cavity by a depressed sternum or by retraction of the left lung and pleura If the heart is displaced upward appreciably its apex tends to lie in the fourth intercostal space or behind the fifth rib and may then be normally slightly (½ to 1 cm) beyond the midclavicular line In infants and very young children especially when they are fat the apex impulse is normally often in the fourth intercostal space just beyond the midclavicular line

Certain changes of body position and of the height of the diaphragm cause considerable shifting of the position of the apex impulse when the heart is normally freely movable The three greatest shifts are produced as follows (1) a change from the left to the right lateral decubitus causes a shift of the mediastinum and its contents including the heart laterally, the cardiac apex impulse moving often as much as 4 or 5 cm from left to right, from out toward the anterior axillary line to a point not far to the left of the sternum, such a shift does not markedly affect the angle of either the anatomic or the electric axis and so produces little change in the electrocardiogram which in part explains why such a test of change of position is of little value in the diagnosis of adhesive pericarditis (2) A change in the height of the diaphragm produced readily by deep breathing alters appreciably the position of the apex impulse both laterally and vertically from say a point in the midclavicular line underlying the fifth rib to a point 1 to 1½ cm inside the midclavicular line underlying the sixth rib such a shift does markedly affect the angle of both anatomic and electric axes of the heart and so produces usually a striking change in the electrocardiogram particularly in Lead 3 (see Figure 4 page 33) (3) A change from the supine to the standing position alters somewhat the position of the apex impulse partly by straightening out the heart (that is in slight to moderate degree making it more vertical), partly by producing a rotation from left to right and partly by causing a drop of the heart as a whole the result is somewhat like that caused by deep inspiration but not so pronounced and more complicated in mechanism the effect on the electrocardiogram is very variable but usually not marked (see Chapter 9)

Finally it is to be noted that the nipple line is not a suitable guide to heart size chiefly because of its great variation in distance from the midsternum in

individuals of the same size (as much as 2 or 3 cm in extreme cases) but also because as a rule its position is normally 1 to 2 cm beyond the site of the cardiac apex

The major pulsatory movements of the thoracic wall which may be seen and felt resulting from the action of an enlarged heart are often complicated but their analysis may aid in elucidating the heart condition they have been made the subject of a monograph by Dressler (1933 and 1937) A few major points of interest are the rocking movement of the thorax when the left ventricle is very large and forceful the left thoracic wall moving outward and the right inward in systole and vice versa in diastole the forward thrust of the anterior thoracic wall with retraction of both lateral walls in systole when the right ventricle is very large and strong together with a visible and palpable forceful impulse in the region of the pulmonary artery in some such cases when the chest wall is not too thick and an outward thrust of the right chest wall in systole when the atria are markedly enlarged as in the case of the occasional huge left atrium found in advanced mitral valve disease and of the large right atrium in tricuspid valve disease the outthrust being due not to atrial contraction but to the forceful ventricular pulse transmitted directly into the atrium through the incompetent valve These are more or less major pulsatory movements in addition to the apex impulse itself When the heart is much enlarged and its action forceful the fifth and sixth ribs are outwardly displaced at each heart beat

Two other points about cardiac pulsation are worthy of comment First a very active heart whether enlarged or not will produce such a forceful apex impulse that it is widely felt and may be misleading it is the maximal point of this impulse or rather a few millimeters beyond but not its furthest point out that marks the position of the apex itself Second a systolic retraction of the fourth and fifth intercostal spaces just to the left of the sternum often well seen in a person with a thin chest wall is a normal occurrence when the heart is not enlarged or when only the left ventricle is enlarged and it is not to be interpreted as the result of pericardial adhesions it is due to the withdrawal of the right ventricle from the chest wall when it contracts against the left ventricle which in turn contracts away from the region of the sternum but thrusts its apex up against the chest wall further to the left that is in or beyond the midclavicular line depending on the size of the left ventricle

Thrills The next observation to make in physical examination of the heart is to palpate the precordium for thrills which are often difficult to feel with the untrained hand unless they are very marked in degree exercise by increasing heart action and blood flow helps to make thrills that are faint more evident when a thrill is suspected and is not brought out by exercise it probably does not exist Thrills are relatively rare accompanying a few murmurs only especially the aortic systolic murmur of aortic stenosis and the mitral diastolic murmur of mitral stenosis Valvular regurgitation produces thrills in only the rarest cases whether from aortic regurgitation mitral regurgitation or pulmonary regurgitation and then usually when the valve has an odd deformity

such as eversion or rupture of an aortic cusp or a rupture of mitral cusp or of chordae tendineae

A systolic thrill felt over the precordium but best in the second intercostal space just to the right of the sternum (so-called aortic valve area) and transmitted into (but not limited to) the vessels of the neck is due as a rule to aortic or subaortic stenosis rarely to an aortic aneurysm, it is of interest and importance that such a thrill may be felt well also at the cardiac apex A systolic thrill, felt usually in a narrowly localized area in the second inter costal space just to the left of the sternum (so-called pulmonary valve area) means in most instances congenital stenosis of the pulmonary valve or of the infundibulum of the right ventricle rarely patency of the ductus arteriosus or extreme dilatation of the pulmonary artery A systolic thrill also usually very limited in extent felt in the fourth intercostal space just to the left of the sternum indicates as a rule the presence of an interventricular septal defect A diastolic thrill middiastolic or presystolic in time felt in a small area at the cardiac apex and a little toward the midsternum from the apex is characteristic of a high degree of mitral stenosis but is also found in rare cases of marked dilatation of the left ventricle with rapid blood flow (see Chapter 14) A continuous thrill rather rare felt in the second intercostal space just to the left of the sternum is found in a few cases of patency of the ductus arteriosus or to the right in the extremely rare instances of right aortic arch or dextrocardia plus patency of the ductus arteriosus such a thrill is also characteristic of an arteriovenous communication (called aneurysm) any where in the body

Finally it should be noted that the search for thrills may be misleading for three important reasons (1) they may not be felt even in the presence of loud and important murmurs as for example in some cases of aortic stenosis (2) they may be suspected when there is actually nothing wrong and (3) they may be felt in almost unique cases where no murmur can be heard due to the inaudibility of vibrations of very low pitch which are never theless of importance

PERCUSSION

Before turning to the subject of cardiac auscultation later in this chapter I welcome the opportunity to say a few words about the much neglected and often despised method of cardiac percussion (*percutere* to strike) Percussion of the heart is valuable in the first place because it aids in determining heart size and shape when it is not possible to carry out a roentgen ray study a procedure that continues to be difficult or impossible in the case of quite a few patients Secondly it is of help in occasional cases when the apex impulse is felt with difficulty or not at all And thirdly it serves as a check on the accuracy of reports of roentgen ray measurements Considerable train ing and experience are necessary before one can properly rely on the accuracy of cardiac percussion but such training and experience are not difficult and

they are well worthwhile The method of percussion matters little that is whether direct (immediate) or indirect (mediate) whether one uses the finger or special instrument as the pleximeter and whether a hard stroke or a gentle stroke is employed (a light stroke is preferable when the chest wall is thin and the heart near to its surface and a heavier stroke when the chest wall is thick or some emphysema of the lungs is present) The main point is to adopt a definite technic and to stick to it until one becomes expert in its use constantly comparing at first the results obtained with the heart measurements by orthodiagram Percussion involves not only the sense of hearing but also that of touch

Auenbrugger Leopold *Inventum Novum Ex Percussione Thoracis Humani* Vienna 1761

From John Forbes English translation 1824

I The thorax of a healthy person sounds when struck

II The sound thus elicited from the healthy chest resembles the stifled sound of a drum covered with a thick woollen cloth or other envelope

III Over the space occupied by the heart the sound loses part of its usual clearness and becomes dull

IV The thorax ought to be struck slowly and gently with the points of the fingers brought close together and at the same time extended

Scholium Robust and fat subjects require a stronger percussion such indeed as to elicit a degree of sound equal to that produced by a slight percussion in a lean subject

X To be able justly to appreciate the value of the various sounds elicited from the chest in cases of disease it is necessary to have learned by experience on many subjects the modifications of sound general or partial produced by the habit of body natural conformation as to the scapulae mammae the heart the capacity of the thorax the degree of fleshiness fatness and so forth

XLVI Signs of Hydropericardium The sound in the cardiac region is now as completely deadened as if the percussion were applied to a fleshy limb

XLVIII When the heart becomes so much distended by blood accumulated in its auricles and ventricles as to be unequal to propel forward its contents it frequently becomes thereby enormously dilated This dilatation has been called Aneurism of the Heart

The pathognomonic sign of this affection is the complete fleshy sound on percussion existing over a considerable space in the region of the heart

In the course of one s palpation and percussion one may elicit an important symptom namely *precordial tenderness* which in the absence of local trauma or lesion of the chest wall itself is useful evidence of a high degree of nervous sensitivity or fatigue as in cases of neurocirculatory asthenia it is found usually in the absence of heart disease (see Chapter 22)

It is well to percuss first the cardiac apex beginning in the left axilla and working toward the sternum One observes a pronounced change of note and resistance when one reaches the apex (usually 7 to 9 cm to the left of the

midsternum in the normal adult) and this point agrees within a centimeter with that of the maximal apex impulse it tends to be a few millimeters further to the left It is to be compared as is the site of the apex impulse with the midclavicular line Next it is best to percuss the left border of the heart in the third and fourth intercostal spaces an increase of heart size toward the left is usually made out readily and here again there is close agreement as a rule between percussion and orthodiagraphic measurements

Percussion dullness in the third intercostal space to the left of the sternum should not normally exceed one half the distance from midsternum to apex (that is not more than 3½ to 4½ cm according to the size of the individual) it often measures less If it does exceed this we have evidence of abnormality in heart size or shape or both It may be too far to the left even when the apex impulse is in the normal position such a finding is usually indicative of mitral stenosis an atrial septal defect or congenital patency of the ductus arteriosus for the measurement records the size of the left atrium near its appendage and of the trunk of the pulmonary artery

The reason why the left border of the heart can be so well percussed in most cases is because it lies close to the anterior chest wall especially in the sitting and standing positions Obesity and pulmonary emphysema and rarely widely transmitted abdominal tympany may interfere with percussion of the heart

We find a very different situation when we try to percuss the great vessels in the first and second intercostal spaces to left and right of the sternum and under the upper sternum itself It is difficult or impossible to outline these structures when they are normal and sometimes even when they are enlarg d because of their small size, their distance from the anterior chest wall and their proximity to resonant air passages and lung apices Only when there is a pronounced abnormality as in the case of an aortic aneurysm does one find increased dullness by percussion to the right or left of the upper sternum respectively It is generally convenient to make a record that there is no abnormal dullness in the region of the great vessels except in the infrequent cases where there is such abnormal dullness rather than to attempt to distinguish doubtful percussion borders The same is true of percussion of the right side of the heart in the attempt to outline the position of the border of the right atrium, it is impossible to percuss accurately this heart border because of its distance from the anterior chest wall there being an error of 1 to 1½ cm under the best of circumstances (the right border of the right atrium in the normal adult is usually about 4 cm to the right of the midsternum while the dullness by percussion extends only 2 to 2½ cm to the right just barely beyond the right edge of the sternum) Clearly defined dullness to percussion in the third and fourth intercostal spaces more than a centimeter to the right of the right edge of the sternum almost always means enlargement of the heart in whole or in part or displacement of the heart to the right or a pericardial effusion rarely this may be found normally when the chest wall is very thin As a rule therefore it is convenient to say that there is no ab-

normal dullness to the right of the sternum when such is true rather than to give measurements which are misleading as to actual heart size

Finally we need no longer trouble with the old designations absolute and relative cardiac dullness they serve no useful purpose

AUSCULTATION

Laennec R T H *De l'auscultation mediate* Paris 1819 Brief extracts translated by myself

About three years ago I began the research the result of which I am publishing today

Some physicians have tried to apply their ears to the precordial region in these cases The heart beat perceived thus simultaneously by the senses of hearing and of touch becomes more evident This method is however far from giving the results it would seem to promise I have found it advised nowhere As uncomfortable for the physician as for the patient the method is so disagreeable that it is practically of no use in the hospitals it is hardly to be suggested in the case of most women and in some of them it cannot be employed at all because of the size of the breasts

I was consulted in 1816 by a young woman who presented general symptoms of heart disease and in whose case the application of the hand and percussion gave little information because of her obesity Since the age and the sex of the patient forbade my using the method of examination already described (that is immediate auscultation) I happened to recall a well known acoustic phenomenon if one applies the ear to one end of a beam one hears very distinctly a pin scratch at the other end I thought that I could profit by this physical property in the case of the patient under discussion I took a sheet of paper rolled it up tightly applied one end of this cylinder on the precordial region and placing my ear against the other end I was as surprised as pleased to hear the heart beat in a manner much more clear and distinct that I had ever done by applying the ear immediately to the chest

I use at present a cylinder of wood pierced in its centre by a tube three lines in diameter and divided in the middle by a screw joint in order to make it more portable

Auscultation of the heart (*auscultare* to listen) has become a time worn method of examination and is considered by some to be old fashioned and unworthy of especial attention but it remains today a source of vital information about the heart and it has actually advanced in importance in the last two decades because of the better understanding of its findings Like percussion it demands careful training and long experience for its mastery but the time spent on it is exceedingly worthwhile Because of our present knowledge about heart sounds and murmurs even direct or immediate auscultation may be practiced with far better success than in the days before Laennec introduced the stethoscope for indirect or mediate auscultation in 1819 but the use of the ear directly applied to the chest is clumsy and inconvenient and does not allow the detection of the fine shades of tone and intensity that is

possible by the use of a stethoscope The most useful instrument is binaural with two easily adjustable chest pieces one a bell and the other a flat resonating chamber with diaphragm (Bowles chest piece) which have a somewhat selective action For physicians who are hard of hearing and for amphitheater clinics audion tube amplifiers are now available With earphone connections there is very little distortion of sounds and murmurs this method has proved to be well worthwhile in demonstrations to large groups during the past few years

Auscultation of the heart should be carried out at the cardiac apex (mitral valve area) in the second intercostal space just to the right of the sternum (aortic valve area) in the second intercostal space just to the left of the sternum (pulmonary valve area) at the left of the mid and lower sternum (septal and tricuspid valve areas) and in the left axilla lung bases and neck for transmission of murmurs Both bell and Bowles chest pieces should be used and if there is any possibility of mitral stenosis and the murmur thereof is not heard with the subject in the upright position it should be sought with the subject supine or lying on the left side and after exercise It is also worthwhile to listen routinely over the thoracic spine in a search for the continuous murmur caused by coarctation of the aorta

An interesting application of the principle of selective binaural timing of sounds and murmurs to ascertain their points of origin and directions of transmission for example from cardiac base toward apex or vice versa has been introduced and perfected by Kerr and his associates (1937) this acoustic principle is similar to the optic recognition of distances and timing by binocular perspective vision The instrument devised for this purpose has been called the symballophone and can be used helpfully provided the hearing is equal in both ears (they should be accurately tested) and provided experience in the use of the symballophone is gained by practice inertia has delayed any general adoption of this innovation

Phonocardiography (also called stethography in the past) the graphic recording of heart sounds and murmurs by electric reproduction using microphone amplifier and galvanometer has gradually reached a good state of development during the past generation and can usefully supplement the personal use of a stethoscope by a trained observer especially in the exact timing of sounds and murmurs in problem cases Two difficulties have yet to be eliminated the first that of the frequent addition of artifacts from extraneous sounds or electric currents to the heart sound records and second that of the sometimes inadequate reproduction of certain murmurs especially the fainter diastolic murmurs of low or high pitch However these difficulties have been largely surmounted One additional benefit may eventually accrue through this technical method of study namely extra information about the state of the heart from variations in inaudible vibrations picked up by the apparatus but which have not as yet received adequate clinical analysis Classroom amplification of heart sounds and murmurs by the additional use of a loud speaker needs further perfection

There were published some years ago (Rappaport and Sprague 1941 and 1942) two interesting and valuable papers on the physiologic and physical laws that govern auscultation and their clinical applications with especial reference to phonocardiography their conclusions are worthy of direct quotation Their 1941 paper was summarized as follows

Rappaport Maurice B E E and Sprague Howard B M D Physiologic and Physical Laws that Govern Auscultation and Their Clinical Application *Am Heart J* 1941 XXI 257

"1 Tones of different periods of oscillation or frequency but of similar intensity affect the human ear to different degrees The audiogram which is a graphic representation of the threshold of audibility is a measurement of the degree to which human hearing varies with respect to the frequency of vibration of the stimulus

"2 The minimum change in intensity of a sound stimulus to which the human ear is capable of responding varies with the general level of the sound as well as with *its frequency In the auscultatory frequency band as the frequency of the* stimulus is lowered a decidedly greater percentage variation in intensity is therefore required to produce the minimum perceptible change

"3 The human ear is a better detector of changes in frequency than of changes in intensity A sound stimulus with a high sensation level requires less of a frequency variation to produce minimum susceptibility than does a sound stimulus of a lower sensation level Also the ear is somewhat less sensitive to frequency variations at the lower end of the auscultatory frequency band than it is to variations in the upper region

4 In the auscultatory frequency band the frequency of a stimulus may be varied rapidly over a considerable portion of an octave without detection by the ear

5 The auditory sensation produced by a complex sound may be decidedly different in character as well as in intensity when the stimulating level is decreased or increased even though no distortion is introduced As a complex sound such as a murmur becomes more intense the low pitched components appear more prominent to the observer

6 When a sound of comparatively high intensity immediately precedes a sound of considerably lower intensity masking of the sound of lower intensity may result.

7 There are many paths along which heart and chest sounds travel in the human body in order to reach the surface As a result a large percentage of the sound energy never reaches the surface because of viscosity elasticity density spreading reflection and refraction losses

8 The entire auscultatory frequency band for heart sounds and murmurs lies below 1 000 cycles per second An estimation of the lower frequency limit of heart sounds and murmur components puts it in the vicinity of 5 to 10 cycles per second although 30 to 40 cycles per second is the lower limit of audibility

9 Acoustic stethoscopes may be classified as either monaural binaural or differential Either the monaural or binaural stethoscope may be employed for general auscultatory purposes whereas the differential stethoscopes are primarily instruments for localizing and comparing sounds

10 The open stethoscopic chest piece or bell when applied to the patient s

chest may be considered as a diaphragm type of chest piece The skin which bounded by the lip of the bell forms the diaphragm and the fleshy portion und the skin acts as a damping medium

11 The larger the diameter of the open stethoscopic chest piece the better i response to low pitched sounds This is accomplished at the expense of the highe frequency components

12 The greater the pressure with which the open stethoscopic chest piece i applied to the patient s chest the better is the response of the stethoscope t higher frequency components Thus by varying the application pressure th physician exerts a variable filtering action upon the sounds because the natur period of the skin diaphragm bounded by the chest piece depends on the applicatio pressure

13 Open stethoscopic chest pieces of various geometrical shapes have bee devised to improve the sound accumulating efficiency of the stethoscope A be with its interior shaped like a parabola has been a favorite Such chest pieces in variably decrease the efficiency of the stethoscope because they increase th internal volume of the chest piece

14 The only important consideration when designing an open stethoscopi chest piece is to keep its internal volume at a minimum and have it so shape that in the case of an obese patient or one with an inelastic chest wall the bel will not fill with flesh to such an extent as to decrease effectively the diameter o the enclosed diaphragm

15 The diaphragm type of chest piece (Bowles type) which is commonl used in auscultation is especially useful in detecting faint high pitched sounds When it is applied to a patient s chest the principle of operation of the Bowle chest piece is similar to that of the open bell except that additional attenuatior of the lower pitched heart and chest sound components is obtainable with th Bowles chest piece and this prevents masking of the higher pitched components

16 In the Bowles chest piece as in the open type of chest piece the ai volume should be made as small as possible in order to obtain maximum efficiency

17 Between 60 and 400 cycles per second which includes most of the ausculta tory region tests show that the binaural method of auscultation through rubber tubes is on an average 20 decibels better than the monaural method with the ear directly applied to the stethoscope A 20 decibel difference is equivalent to a tenfold increase in sound pressure at the ear drum Only between 850 and 1 000 cycles per second is monaural or direct auscultation more efficient than binaural and this range is too high to be practically useful

18 The changes in the efficiency of an acoustic stethoscope which are caused by varying the length of the tubing although they are not given any consideration by stethoscope users produce an effect upon the quality of sounds Tests show that below 100 cycles per second the efficiency is not materially affected by tubing length Between 100 and 1 000 cycles per second tubing length exerts a con siderable effect that is the efficiency decreases with increased tubing length This efficiency loss occurs in the region of the low intensity high pitched diastolic murmurs and every possible increase in efficiency in this region is of utmost valu

19 In order to obtain the most efficient tubing dimensions one should make the tubing as short as possible and compromise on the resistance and volume com ponents The compromise may be approached by plotting a graph representing efficiency versus volume effect and another representing efficiency versus fric

tional resistance effect where the two curves intersect is the point of optimum efficiency

20 For general clinical use an electrical amplifying stethoscope must transmit sounds to the observer with a quality and fidelity equal to that of the average acoustic stethoscope A modification of the frequency response characteristic of an electrical stethoscope will definitely alter the quality and character of the sounds

21 An amplifying stethoscope is not primarily an instrument to be used for making sounds many times louder than they can be heard with an acoustic stethoscope The major advantage of the amplifying stethoscope over the acoustic stethoscope is that it enables one to adjust the intensity to the desired level and thus eliminate a number of modifying characteristics peculiar to human hearing which cannot be overcome with the acoustic stethoscope

22 When filters either electrical or acoustic are used with an amplifying stethoscope they should possess frequency response characteristics similar to those of the various open and diaphragm chest pieces

23 For teaching purposes a loud speaker may be used in conjunction with ie amplifying stethoscope The over all frequency response of the loud speaker nd amplifying stethoscope must be identical with that of the average acoustic ethoscope in order not to modify the quality and character of the sounds

24 In order to maintain an identical and known relationship between sounds s heard and as recorded the recording galvanometer and audiophone must be ed from the same source that is the same electrical pulsations which pass to the udiophone are fed into the galvanometer

The 1942 paper by Rappaport and Sprague was entitled The Graphic Registra ion of the Normal Heart Sounds *Am Heart J* 1942 XXII 591

1 When a patient is ausculted in the usual stethoscopic manner the observer loes not hear the cardiac vibrations as they actually exist at the source because of hree major forms of modification namely

a The heart sounds are altered in their transmission from the source to the surface of the chest

b The heart sounds that reach the surface of the chest are additionally modified by the acoustic stethoscope and the type of chest piece employed

c The observer does not perceive the heart sound vibrations as they are transmitted to the ears by the acoustic stethoscope

2 The three major forms of cardiac sound modification are related to ausculta ion as follows

a The chest transmissional factor must be considered and handled as a variable quantity

b Modification effects that are introduced by acoustic stethoscopes and their chest pieces may be made non variable No attempts at stethoscopic stand ardization have as yet been made Until such standarizations are accomplished the stethoscopic factor must be considered as a variable quantity in auscultation

c Modification effects that are introduced by average normal hearing may be considered as a constant quantity in auscultation with the condition that personal factors such as auscultatory experience fatigue surrounding noise level and rhythmic concentration ability are omitted

3 The three major forms of cardiac sound modification that are encountered in auscultation may have the following relationships to phonocardiography

a In phonocardiography as in auscultation the chest factor must be considered as a variable quantity

b The modification effects that are introduced by an acoustic stethoscope and its chest pieces in auscultation may be reproduced perfectly by phonocardiography

c The logarithmic type of modification that is introduced in auscultation by average normal hearing may also be reproduced by phonocardiography

4 Phonocardiographic registration may therefore be considered according to the degree of modification introduced namely

a Linear phonocardiography or the registration of the sound vibrations as they exist on the surface of the chest

b Stethoscopic phonocardiography or the registration of the sound vibrations as they are transmitted to the ears by an average acoustic stethoscope

c Logarithmic (human audiographic) phonocardiography or the registration of sound vibrations as they are perceived by a competent observer if the personal factors are omitted

5 Linear stethoscopic and logarithmic phonocardiography are directly related to auscultation Each phonocardiographic method is a representation of a definite stage of sound transmission in auscultation Deviations may be introduced by a phonocardiograph with frequency response characteristics other than linear stethoscopic or logarithmic Such deviations bear no direct relationship to the auscultatory transmission and detection stages Therefore a phonocardiograph with other than linear stethoscopic or logarithmic characteristics must be considered as either an apparatus of poor design or an expression of the designer's personal opinion unless the deviation is based upon a natural constant

6 The linear phonocardiograph is essentially an electrical sphygmograph which possesses several advantageous characteristics not common to the segment capsule or direct optical type of sphygmograph

7 A linear phonocardiogram when registered over the apex is an apex cardiogram or apex beat tracing

8 A chest piece was devised which makes possible simultaneous phonocardiographic registrations over the same precordial area For example this dual chest piece is useful for simultaneously registering the apex beat and the stethoscopic or logarithmic phonocardiogram at the apex Clinically such simultaneous registrations may be useful in differentiating between the third heart sound and the opening snap of the mitral valve when the isometric relaxation phase of the left ventricle is shortened by mitral regurgitation The apex cardiogram is also useful in timing diastolic events as in venous pulse registration In some persons it is rather difficult to record the venous pulse in such cases the apex cardiogram may be registered instead

9 The first heart sound is composed of four components namely

a The first which is caused by residual vibrations of auricular origin

b The second which is produced at the beginning of the isometric contraction phase of the cardiac cycle (closure of the mitral and tricuspid valves)

c The third which is caused by the opening of the semilunar valves

d The fourth which is caused by the acceleration of the blood in the arterial vessels during the maximum ejection phase of ventricular systole

10 The linear phonocardiograph is capable of registering the first and fourth

components of the first heart sound efficiently but is very inefficient in the registration of the second and third components

11 The stethoscopic phonocardiograph registers the first and fourth components of the first heart sound with some attenuation but does not obliterate the vibrations The second and third components are registered distinctly

"12 The logarithmic phonocardiograph obliterates the first and fourth components of the first heart sound of most normal persons and registers the second and third components distinctly

"13 When a normal person is ausculted the observer rarely hears the first and fourth components of the first heart sound the second and third components are well heard Logarithmic hearing (as indicated by logarithmic phonocardiography) is responsible for this auscultatory condition because of the greater relative attenuation of the low frequency first and fourth components than of the higher frequency second and third components Logarithmic attenuation of the first and fourth components is of sufficient magnitude to bring them below the level of human audibility

14 A simultaneous stethoscopic or logarithmic phonocardiogram and venous pulse tracing may serve as a means of differentiating between a prolonged first heart sound and a first heart sound which is followed by a short systolic murmur In the latter instance it extends beyond the c wave peak

15 Our observations indicate that the second normal heart sound may be composed of four components namely

a The first vibrations which represent the beginning of the diastolic fall in pressure with ventricular relaxation

b The second group of vibrations which are caused by the closure of the semilunar valves (termination of ventricular systole)

c The third group which are most likely due to the arterial wall and blood column vibrations An additional possible source of vibration in this phase of the second heart sound may be the natural period vibration of the chest wall which may conceivably be set into oscillation by the second component

d The fourth component is caused by the opening of the mitral and tricuspid valves

16 The logarithmic phonocardiogram almost always totally obliterates the first third and fourth components of the second heart sound vibrations whereas the stethoscopic and linear phonocardiogram may show all four components This indicates that no matter how competent an observer may be he can hear only the second component of the second heart sound of a normal person because his hearing is logarithmic

17 Although the duration of the normal second heart sound is nearly equal to that of the first, auscultation makes the second sound appear shorter This is explained by the fact that normally two components are audible in the first heart sound whereas only one is audible in the second heart sound

"21 For maximum accuracy in all types of phonocardiographic analysis a phonocardiograph capable of registering the heart sounds linearly stethoscopically and logarithmically should be employed

Thus it becomes evident that much of the discussion about phonocardiography in the clinic in the past has been unsound because of the failure to

recognize the important differences between the various types of phonocardiograms mentioned above namely the linear the stethoscopic and the logarithmic which not infrequently have been erroneously compared as if they were the same in detail Despite the importance of their distinction it is possible that many of the vibrations that are inaudible but that can be recorded may in their variations eventually prove to have almost as much clinical significance as the heart sounds and murmurs themselves this is for future studies to determine Figure 12 illustrates two of the three types of phonocardiogram—stethoscopic and logarithmic—in the same case (see below)

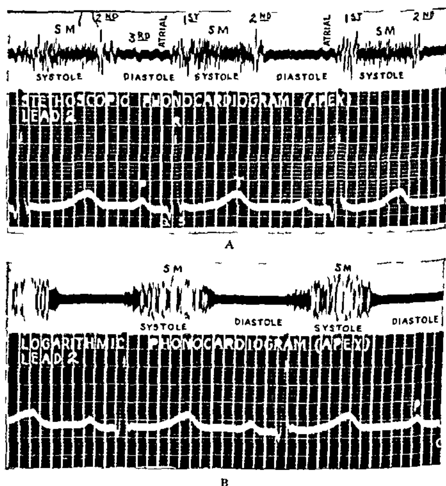


FIG 12 Comparison of stethoscopic and logarithmic phonocardiograms (*A* and *B* respectively) taken at the cardiac apex in the same individual with loud systolic murmur It is of interest to note in the stethoscopic phonocardiogram the third and the atrial sounds which are not audible to the human ear and are not shown in the logarithmic phonocardiogram also the difference in the records of the murmur is quite obvious (Kindness of *Mr M A Rappaport Sanborn Company Cambridge*)

HEART SOUNDS

There are normally three heart sounds but the third is often very faint or even inaudible The first sound loudest at the apex is produced by closure of the mitral and tricuspid valves plus an element of muscular contraction and roughly marks the beginning of systole at its very beginning and merged with it is a very short presystolic phase due to atrial contraction which audible or not is indistinguishable from the first sound itself unless there is abnormal lengthening of the interval between the atrial and ventricular contractions The second sound usually loudest at the base in the pulmonary valve area in children and young adults and in the aortic valve area in the middle aged and elderly is produced by closure of the aortic and pulmonary valves roughly marking the beginning of diastole The third sound in the normal subject heard as a rule best at the apex and thence halfway to the left sternal border when it is audible at all is probably the result of the vibration of the ventricular walls and atrioventricular valve cusps caused by the inrush of blood in every diastole it is best heard in children after exercise and in the recumbent position It occurs early in diastole about 0 1 second after the second sound The opening snap of the atrioventricular (chiefly the mitral) valves if heard at all forms but a late part of the second sound or at most reduplicates it it comes definitely earlier than the time of the third heart sound

The heart sounds are proportionately increased in intensity when the chest wall is thin and as the result of increase in blood flow by exercise excitement or certain drugs They are proportionately decreased by a thick chest wall pulmonary emphysema and a state of weakness prostration or shock

First heart sound The first sound is *accentuated* at the apex when the heart action is forceful and the blood flow is rapid as normally after exercise or excitement and abnormally in thyrotoxicosis and in some cases of neurocirculatory asthenia it is most accentuated in the presence of mitral stenosis with forceful heart action It is not primarily accentuated at the base but it may be so at the lower end of the sternum in very rare cases of tricuspid stenosis

The first sound is *diminished* at the apex and secondarily at the base in the presence of great myocardial weakness and failure and temporarily when there is a state of vasomotor shock approaching then the usually lesser intensity of the second sound at the apex it gives rise to tic tac rhythm Extreme weakness of the first heart sound is a bad sign

The first sound may be *masked* by a systolic murmur either at apex or base The most complete obliteration of this sort is by the harsh systolic murmur of aortic stenosis

The first sound at the apex may be delayed by the hemodynamic conditions that exist in mitral stenosis occurring a perceptible interval after the beginning of the apex impulse itself (Cossio 1943)

Finally the first sound may be *reduplicated* such reduplication is best heard

at the apex and results from either (1) an asynchronism of the closures of the mitral and tricuspid valves, due to asynchronism of left and right ventricular contractions as in bundle branch block or to other cause of change in the intraventricular and intra atrial pressure relations or (2) a delay in atrioventricular conduction (first grade of heart block) whereby the atrial contraction sound precedes the first ventricular sound by a small fraction of a second

Second heart sound The second sound is not primarily accentuated or diminished at the apex Its *accentuation* at the aortic valve area with the subject at rest is commonest in cases of systemic hypertension especially *hyperpiesia but it is occasionally louder than normal and metallic in character* when there is dilatation of the aorta in syphilitic aortitis and with marked arteriosclerosis Accentuation of the second sound in the pulmonary valve area may be normally produced by exercise and by deep expiration particularly if *the subject is supine if it is accentuated with the subject at rest* and breathing quietly it is a sign of pulmonary hypertension due most commonly to weakness and failure of the left ventricle occasionally to mitral stenosis and rarely to acute or chronic obstruction in the pulmonary circulation itself (as in the acute and chronic cor pulmonale—see Chapter 20) or to congenital defects especially an atrial septal defect A point of great importance is the relationship between the intensity of the aortic and pulmonary second sounds In an older person and in a patient with systemic hypertension without heart failure the aortic second sound is greater than the pulmonary second sound When in such individuals the sounds become equal in intensity or the pulmonary second sound becomes the louder we have evidence of pulmonary hypertension this in the case of systemic hypertension means weakness and failure of the left ventricle Recovery from the heart failure is attended by a return of the intensity of the pulmonary second sound to a level below that of the aortic second sound

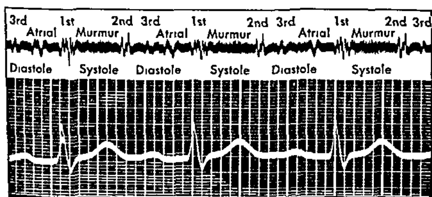
The second sound is primarily *decreased in intensity* to an important degree chiefly at the aortic valve area This is found particularly with aortic stenosis when *the sound may be entirely absent and temporarily with a state of* vasomotor shock With congenital pulmonary valve stenosis the pulmonary second sound may be much diminished or rarely absent *It is to be observed* however that the second sound heard at either aortic or pulmonary valve area *may be transmitted to that point from the other side of the sternum* this fact has been inadequately recognized and noted

The second sound may be *masked* by a loud early diastolic murmur at the aortic valve area and along the left border of the sternum in occasional cases of marked aortic regurgitation

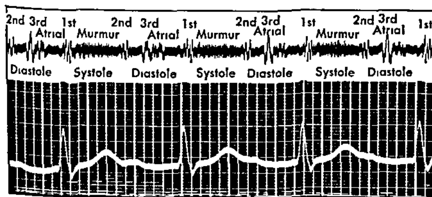
Reduplication of the second heart sound is maximal at the base and is due to asynchronous closure of the aortic and pulmonary valves as the result of a disturbed balance of blood pressure relations between the ventricular cavities on the one hand and the aorta and pulmonary artery on the other hand or of asynchronous contraction of the ventricles as in bundle branch block Re

duplication of the pulmonary second sound is quite common and like the pulmonary systolic murmur may be produced in the normal individual by deep expiration in the supine position When well marked with the subject at rest it is like accentuation of the pulmonary second sound suggestive of mitral stenosis The opening snap of the mitral valve if accentuated may reduplicate the second sound at the cardiac apex

Third heart sound *Accentuation* of the third sound or the appearance of an extra sound early in diastole (Figure 13) may be caused in slight degree by



A



B

FIG 13 Stethoscopic phonocardiograms showing in *A* with normal *P R* interval normal occurrence of first second third and atrial sounds (and a systolic murmur) and in *B* with prolongation of the *P R* interval in the same case the superimposition of third and atrial sounds to give a summation effect (Kindness of Mr M A. Rappaport, Sanborn Company Cambridge)

exercise when marked it is the result of one of three underlying causes (1) most commonly dilatation of either ventricle (2) mitral stenosis or (3) delay in atrioventricular conduction so that the atrial contraction sound falls with it to reinforce it When the third or extra diastolic sound is loud there

is usually a palpable or even visible extra cardiac impulse accompanying it.

Infrequently one hears an extra sound in systole a snap or twang shortly after the first sound and heard best at the cardiac apex It is a curiosity of academic interest only being found as a rule in healthy individuals without heart disease three cases showing this anomaly and diagnosed correctly ante mortem were reported by Huchard (1893) to have had anomalous chordae tendineae that were undoubtedly the cause of the extra sound an instance of interposition of the atrial contraction in the midsystolic phase has also been noted (Hinohara 1941)

Gallop rhythm Gallop rhythm is the descriptive term that has been applied to the auscultatory finding of a well heard extra sound whether in systole or diastole when the heart rate is rather fast, that is 100 or more Its significance is indicated by the factors responsible for the extra sound as outlined above

Gallop rhythm is often hard to time but usually it is easy to distinguish between the systolic and diastolic varieties The former is rare the latter is common In turn *diastolic* gallop rhythm is divided when possible into protodiastolic and presystolic in timing but often it is impossible even with graphic records in the presence of considerable tachycardia to decide which is which and one has then to be content with the simple designation diastolic"

Protodiastolic gallop rhythm that is the kind with the loud third sound early in diastole if it can be so timed when located at the cardiac apex is usually a serious sign since left ventricular dilatation is the commonest accompaniment of marked accentuation of the third sound A protodiastolic gallop rhythm may be heard best at or be limited to the precordium just to the left of the mid or lower sternum in such cases great right ventricular strain is usually very evident and the gallop is probably the result of dilatation of the right ventricle

A *presystolic* gallop is less serious than a protodiastolic gallop it is found when there is slight delay in atrioventricular conduction or in certain cases with very forceful atrial contraction (in chronic hypertension for example)

A *systolic* gallop is of no clinical importance although it may be present in heart disease

In rare cases four heart sounds are heard with each heart cycle the first second, and third sounds and a presystolic sound (produced by atrial systole)

Atrial sounds Atrial contraction when forceful produces a sound or even a double sound which ordinarily forms a part of and is buried in the regular first sound of the heart when there is delayed conduction or high grade heart block the atrial sound may be faintly audible at the left border of the sternum or at the apex best heard with the bell and with the subject supine (Figure 14)

There are two other points of special interest about heart sounds that deserve mention One of the curious phenomena in medical observation doubtless dating back to the earliest days of mankind many centuries before auscultation either mediate or immediate is the occasional *audibility of the*

artbeat at a distance sometimes with the ear but a few inches from the chest all and sometimes across a wide room One cause of such audibility is left neumothorax another is pneumopericardium and a third is intracardiac nd apparently due to rupture of valve cusp chorda or lax infarcted papillary uscle which allows the mitral valve to slap shut with great suddenness hange of body position and of breathing may greatly affect the degree of udibility

The other point concerns the variation in time interval that may occur even

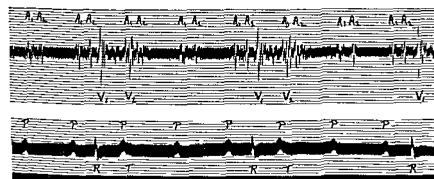


FIG 14 Phonocardiogram (upper tracing) showing double atrial sounds in com plete heart block Electrocardiogram taken simultaneously is shown below Time inter val = 1/30 second (Lewis *Lectures on the Heart* Kindness of Paul B Hoeber Inc New York)

n successive beats between the electric and acoustic records of the heart s action as has been pointed out in two cases of atrial fibrillation (Luisada 1941) the interval was longer after a short diastole

VASCULAR SOUNDS

In the great vessels at the base of the heart and extending into the neck and below the clavicles sounds may be heard which are transmitted from the heart Over the jugular veins especially over the right sided jugular bulb three sounds may be faintly heard if the pulsation there is vigorous and atrial con traction active These three sounds coincide with the three chief waves nor mally seen in the jugular pulse the so called *a c* and *v* waves The first is due to atrial contraction and the other two sounds are undoubtedly the result of transmission of the usual first and second sounds from the heart Other wise the only vascular sound (not murmur) that is audible is that found over any large artery when it is compressed Under certain conditions no com pression is needed to hear this arterial sound occurring with the pulse and due to the sudden tension of the arterial wall these conditions are aortic regurgitation and marked peripheral vasodilatation with vigorous heart action both of these conditions being responsible for the relative emptiness of the arteries at the end of diastole when the next pulse comes through Under such

conditions with compression (or even without it) the sound heard over the greater arteries as over the femoral artery at the groin may be very sharp and has been called the *arterial pistol shot sound*

Finally mention may be made of *fetal heart sounds* which undoubtedly were heard with the ear applied to the abdominal wall long before stethoscopes were invented They are usually faint and so rapid that it may be difficult to distinguish between the first and second heart sounds They are generally well heard with the bell receiver attached to the binaural stethoscope Disturbances of rhythm and rate of temporary significance may be noted and rarely murmurs or arrhythmia of permanent importance such as congenital heart block may be found Little study has as yet been directed to the possibility of diagnosing heart disease from fetal heart sounds although occasional fetal phonocardiograms have been obtained

CARDIOVASCULAR MURMURS

Cardiovascular murmurs like thrills are produced by the vibration of the valves and walls of the heart and great vessels resulting from the rush of blood from a passage of relatively narrow caliber to one of much greater caliber, and by the vibration of a torn or everted valve cusp or of some tissue floating in the blood stream one end of which tissue is fixed to valve or to heart or vessel wall and quite likely by the effect of certain forceful eddies of the blood in its course through the heart Considering the sinuous course of the blood stream it is surprising that murmurs are not routinely found over all hearts whether normal or not rather than that they occur in only a certain number under basal conditions

Speed of blood flow is the most important modifying factor If the flow is fast the murmur will be louder if the flow is slow the murmur will become fainter and if the flow is very slow the murmur may disappear altogether External modifying factors as in the case of heart sounds are common these include obesity and emphysema which diminish the loudness of the murmurs and leanness which increases their loudness In children murmurs are more easily heard than in adults The transmission of murmurs in direction and extent depends partly on the loudness of the murmur partly on muscular and bony conduction in contrast to the damping action of air fluid and fat and partly on the direction of flow of the responsible blood stream

Certain other observations about murmurs are of importance before discussing the individual types Narrowing of a stream of blood without a fairly abrupt dilatation of the caliber of the containing vessel or chamber further on does not cause murmurs Roughening of the surface of the walls of heart or blood vessels does not cause murmurs unless there are appreciable projections or torn fragments to vibrate in the blood stream It is the relation between the calibers of two adjoining parts of the heart or blood vessels and not the absolute size of the caliber of either that determines the production of murmurs For example there may be a loud systolic murmur in the second inter

ostal space close to the sternum if the aorta is dilated even though the aortic alve is normal just as there may be if the aortic valve is stenosed and the iorta of normal caliber Also even though the mitral valve is normal there nay be an apical diastolic rumble if well marked dilatation of the left ventricular cavity (with or without aortic regurgitation) is present just as there nay be if the mitral valve is stenosed and the left ventricular chamber is of normal size The combination of the two factors in either case that is valvular stenosis and dilatation of aorta or of left ventricular cavity favors an increase in the murmur which may be caused by either factor alone

Heart murmurs may be temporary and due to relatively unimportant functional disturbances It is of great importance to recognize and remember that most systolic murmurs do not indicate the presence of any structural or organic heart disease Nevertheless serious diagnoses and bad prognoses have frequently been made largely on the basis of such murmurs On the other hand it should be recognized that even slight systolic murmurs except in the pulmonary valve area may be abnormal they demand study as to their cause Often they are found to be unimportant functional murmurs but frequently they are evidence of the presence of some important or serious disease acting on the circulatory apparatus even though there be no heart disease itself These facts require the application of study and common sense to the interpretation of murmurs and avoidance of the extreme views with overemphasis and underemphasis which have held sway during the swing of the pendulum in the past generation

At this point I would like to urge a revision of the nomenclature of heart murmurs following suggestions published by Adams Craib and myself (1942) The old time worn phrases functional and organic as applied to murmurs are highly unsatisfactory for important reasons in each case Functional has been used equally to signify physiologic and pathologic and even when its interpretation is the latter there is no separation as to extracardiac or intracardiac causation Organic has been in the past limited to structural deformity of a valve even though there may be present much more serious organic disease of the heart than valvular deformity to cause a murmur which has been labeled functional Also it is often impossible to decide at first at least whether valvular deformity or cardiac dilatation without valvular disease is responsible for a murmur even though it is obviously pathologic Therefore we recommend that the terms functional and organic as applied to murmurs be dropped and the designations physiologic and pathologic used instead with proper subdivision of the latter into extracardiac causation as from anemia and intracardiac causation as from myocardial involvement (rheumatic myocarditis myocardial infarction or myocardial failure) on the one hand and valvular deformity (with stenosis regurgitation or both) on the other There may of course be multiple causes for pathologic murmurs in the same case And in those cases in which we cannot tell whether a murmur is physiologic or pathologic we should so indicate

Furthermore it is of great importance to realize that serious heart disease

(or other diseases) may be present in the absence of all heart murmurs, and even with normal heart sounds in some cases Hypertensive heart disease congenital heart disease the thyroid heart syphilitic aortitis and serious coronary disease with or without angina pectoris may be unattended by heart murmurs Moreover some conditions while slight in extent give rise to marked murmurs and when greater in degree they become murmurless This may be illustrated by three instances If mitral regurgitation functional or organic is slight in degree with forceful heart action there is likely to be a loud apical systolic murmur due to the small aperture if this mitral regurgitation becomes very extensive with a very large aperture between ventricle and atrium no murmur at all may be found even though the condition is much worse If a congenital defect of the ventricular septum is small as is the rule a loud systolic murmur with thrill characteristic of the condition results but if the defect is so extreme *that the septum is wholly lacking or only rudimentary there is no resultant* murmur at all while the defect is of course far more serious These facts are easily explained by the first comments made above about murmurs A third example is in the case of stenosis of aortic or mitral valve with well marked murmur when heart failure of serious degree sets in this murmur decreases in intensity and may even disappear in rare cases, moreover the presystolic phase of the mitral diastolic murmur disappears when atrial fibrillation replaces normal rhythm

The intensity of heart murmurs may be very simply and adequately expressed by gradation as follows very slight slight moderate loud and very loud This classification may be expressed by the terms *grade 1 grade 2 grade 3 grade 4* and *grade 5* a very useful procedure as advised by Levine (1933) In addition to notation of the intensity of heart murmurs there should always be a statement as to their exact timing character (blowing rumbling low or high pitched etc) location and transmission The terms constant" and inconstant have no value as applied to heart murmurs to distinguish between pathologic and physiologic types, since some of the former are inconstant and many of the latter are constant

As is the case with heart sounds so on rare occasions very intense heart murmurs may be heard without a stethoscope and with the ear at some distance from the chest wall even the width of a room Such murmurs either systolic *or diastolic in time are in the main very loud and high pitched* and are due to unusual valve deformities, especially rupture of cusps or chordae tendineae

Finally it is to be noted that all murmurs heard over the heart are not intracardiac in origin some are due to the movement of air in the lungs as the mechanical result of cardiac contraction or to the rubbing together of pleural or of pericardial surfaces even though uninflamed

Systolic murmurs 1 *At the cardiac apex* (Figure 12 page 80) The systolic murmur heard at the apex of the heart is commonly blowing in character of moderately high pitch but not as a rule musical beginning with or immediately following the first sound and varying from very short in length and slight in intensity so that it is just recognizable as a murmur rather than as an impure

or slurred first sound to a very long and loud murmur filling all of systole The louder this murmur the wider is the area over which it may be heard Transmission of this murmur to a distance is largely based on the two factors of loudness of murmur and nearness of heart to stethoscope as is true in the case of most murmurs An apical systolic murmur therefore which is trans mitted to the left axilla toward the base of the heart or back of the chest is in the main a loud murmur This type of apical systolic murmur is due to systolic regurgitation of blood through the mitral valve from ventricle into atrium This regurgitation may be the result of organic disease (deformity) of the mitral valve usually rheumatic in origin but this is the rarest of the three usual causes It is more commonly due to organic disease of the heart with dilatation without any deformity of the mitral valve But it is most commonly due to some condition elsewhere in the body which acts by causing a temporary or permanent dilatation of the heart without any real organic cardiac disease or mitral valve deformity such a condition may be either physiologic (if temporary) as after exercise in a rapidly growing child or pathologic as in severe anemia When cardiac dilatation is the cause of the mitral regurgi tation and murmur there are two factors to blame the relative importance of which it is difficult to judge The ring of attachment of the mitral valve may be stretched so that the valve no longer fits tightly or the ventricular dilatation by displacing the papillary muscles downward and outward may prevent the chordae tendineae from stretching sufficiently to allow the valve cusps wholly to close Furthermore it is conceivable that some valves which are originally less perfectly constructed leak with very little provocation In the case of a de formed mitral valve it is the shortening and fusion of the chordae tendineae due to inflammation and cicatrization as well as the defects of the cusps themselves that allow the regurgitation of the blood stream

It is not rare for more than one of the three conditions named above causing mitral regurgitation to be present in the same case as for example coronary heart disease with cardiac weakness and dilatation aggravated by severe anemia

Another known cause for an apical systolic murmur besides mitral re gurgitation is transmission of a systolic murmur from the base or from under the lower sternal region such as occurs commonly in cases of aortic stenosis or dilatation and rarely in cases of interventricular septal defect or pulmonary stenosis Such a transmitted murmur heard at the apex but maximal elsewhere is far rarer than a systolic murmur maximal and originating at or near the apex Uncommonly the harsh systolic murmur of aortic stenosis is better heard at the apex than at the aortic valve area itself A point of much value clinically in distinguishing between the systolic murmurs of mitral regurgitation and of aortic stenosis but relatively slightly known or emphasized is that a loud apical systolic murmur due to mitral regurgitation is well heard in the lung bases in the back but poorly at the base of the heart or in the neck while the aortic systolic murmur is poorly heard over the lung bases and well in the neck and at the cardiac apex

Finally a systolic murmur at the apex is in a few cases obviously due to th movement of air in and out of adjacent or overlying lung tissue caused by th mechanical action of the heartbeat itself or to pericardial or pleural rubbin Cardiac systole may compress lung tissue especially if it is fixed over th heart at the apex and squeeze air out or it may cause a suction of air int lung tissue which had been compressed by the heart in diastole It is generally but perhaps not always possible to differentiate this so called respirator systolic murmur from systolic murmurs of intracardiac origin the respirator character and particularly it variations in different positions of the body an in different phases of respiration (in one of which especially full inspiration it may disappear entirely) and the relative constancy and quality of the intra cardiac murmur usually distinguish between the two Sometimes rales also ar produced in the lungs by the action of the heart causing movement of ai back and forth through moisture in the bronchioles this association of ral production with heart action may help to explain respiratory murmurs presen in the same case The most common form of cogwheel respiration is respira tion punctuated by frequent respiratory murmurs due to the heart s contraction

It has been shown that the rubbing together of uninflamed pericardial o pleural surfaces can produce murmurs mostly systolic but sometimes diastolic (Ortiz 1933) Almost certainly some of the extracardiac murmurs heard clinically are of this origin

There may be other causes for the apical systolic murmur which we do not yet know but certain old terms like hemic and accidental should be omitted Anemia malnutrition and infections act by causing cardiac dilatation and speeding up the blood flow and so produce pathologic murmurs of extra cardiac origin

The time intensity and character of an apical systolic murmur and even the presence of a palpable thrill do not show whether or not the valve is damaged though the loudest murmurs masking the first sound and accom panied by thrills are more often found with valvular disease than without it *When chronic rheumatic heart disease is present with mitral stenosis* the mitral valve lesion may be considered chiefly responsible for the regurgitant murmur and sometimes in young children with a history of recovery from rheumatic fever mitral valve disease may be considered responsible for con stant loud apical systolic murmurs even before mitral diastolic murmurs have developed However is is very important to note that during the acute or *subacute rheumatic infection without previous rheumatic attacks both systolic* and diastolic murmurs originating at the mitral valve are the result of left ventricular dilatation secondary to the myocardial involvement and not to mitral valve deformity which takes in all probability at least a year and more likely two or three to become established sufficiently to cause murmurs (see Chapters 14 and 26)

A word should be added about the time of the apical systolic murmur As a rule the murmur begins early in systole and continues much of the way through if it fills systole it is sometimes called holosystolic The louder and

harsher the murmur the more likely it is to mask not really to replace the first sound In a few cases it begins at an appreciable interval after the first sound or even in mid or in late systole such a late murmur is more likely to be of respiratory than of intracardiac origin but it may be due to the slow yielding in systole of a weak mitral valve ring

2 *At the base* As in the case of heart sounds there is a distinction between systolic murmurs heard in the second intercostal space just to the right of the sternum and in the same space just to the left of the sternum For the sake of convenience these regions have been called the aortic and pulmonary valve areas respectively and they will be so considered here

(a) *Aortic area* There are four chief causes for systolic murmurs heard at the aortic area They are (1) dilatation of the aorta without aneurysm (2) aortic and subaortic stenosis (3) aortic aneurysm (4) transmission of a systolic murmur from pulmonary area from mid or lower sternum or even from the apex The commonest cause of an aortic systolic murmur is simple dilatation of the aorta whether due to chronic hypertension the dynamic effect of aortic regurgitation arteriosclerosis or syphilitic aortitis Upward pressure on heart and great vessels by high diaphragm as in extreme obesity favors the production of an aortic murmur in such cases hypertension is also frequently present A very important and not infrequent cause of an aortic systolic murmur is aortic stenosis which is most commonly of rheumatic or unknown origin rarely due to congenital subaortic or aortic ring stenosis and in more than slight degree only occasionally the result primarily of calcareous disease although calcification is often superimposed on an already damaged aortic valve to increase the degree of its stenosis in the more chronic cases In the case of congenital subaortic stenosis that is of stenosis of the infundibulum or outflow tract of the left ventricle the loud rough systolic murmur may be better heard in the third right intercostal space or even over the sternum itself than in the second space A murmur transmitted to the aortic area from elsewhere is not rare One of the least common causes of an aortic systolic murmur is a saccular aneurysm usually of the ascending aorta or a dissecting aneurysm of the thoracic aorta

The aortic systolic murmur is generally blowing in character except in aortic stenosis when it is harsh and rough It varies in intensity from slight to very loud the latter intensity usually indicating aortic stenosis in which condition the murmur may be so intense that it is heard all over the chest neck and head and even in rare cases with the naked ear a few inches from the chest wall The aortic systolic murmur tends to be transmitted often in its fullest intensity to the cardiac apex itself along the larger arteries and bones into the neck shoulders arms and back (especially down the spine) and even along the abdominal aorta the louder it is the further it is transmitted With a very loud murmur there is usually a palpable thrill most marked when the murmur is especially rough as is often the case with aortic stenosis The time of onset of the murmur is almost invariably very early and if the murmur is loud and harsh it commonly masks the first sound completely The duration

of the murmur is somewhat variable but usually extends throughout systole and in the case of aortic stenosis it is frequently followed by no second sound at all

(b) *Pulmonary area* A systolic murmur at the pulmonary valve area is often found It is the commonest of all heart murmurs and if it is absent with the subject in the upright position it can usually be brought out in the normal individual as well as in the cardiac patient by the assumption of the supine position especially in full expiration Therefore the pulmonary systolic murmur may be considered to be a normal physiologic event unless of considerable intensity in the upright position even then it should be analyzed carefully before being called abnormal The mechanism of this physiologic murmur is not known but it is probably associated with a dilatation of the pulmonary artery under increased pulmonary pressure as in full expiration (or best in the Valsalva experiment which is an attempted forced expiration with the glottis closed) or with a kinking of the artery by change in position or with other factors which may lead to dilatation This physiologic pulmonary systolic murmur is blowing in character begins early in systole but does not mask the first sound extends through most of systole is as a rule not widely transmitted and is associated frequently with accentuation or reduplication of the pulmonary second sound physiologically produced in a similar way

Pathologic dilatation of the pulmonary artery is a much less common but far more important cause of a blowing pulmonary systolic murmur (of varying intensity) than is temporary physiologic dilatation The causes of this pathologic dilatation are (1) pulmonary hypertension most commonly due to failure of the left ventricle but also to mitral stenosis and certain congenital anomalies serious chronic pulmonary fibrosis and emphysema and the rare pulmonary endarteritis (2) thyrotoxicosis which greatly increases the pulmonary blood flow and so dilates the pulmonary artery and (3) rare congenital defects especially an atrial septal defect with resultant flooding of the pulmonary circulation (see Chapter 13) Here as in the case of the physiologic increase of pressure in the pulmonary circulation the pulmonary second sound is often markedly accentuated and may in rare cases be followed by a blowing diastolic murmur which is discussed later in this chapter

Other causes of a pulmonary systolic murmur are rather rare though important Congenital pulmonary stenosis is as a rule but not always accompanied by a loud harsh systolic murmur usually masking the first sound and by a palpable thrill Both murmur and thrill are maximal in the second left interspace near the sternum sometimes a little higher (second rib) and sometimes if the infundibulum of the right ventricle and not the pulmonary valve is stenosed a little lower (third rib or third interspace) Such a difference in site of the maximal murmur and thrill may not however mean a difference in pathologic state The character time relations and intensity of the murmur resemble those of aortic stenosis but the positions differ and the pulmonary stenosis murmur is not so widely transmitted it is sometimes localized to a small area only 2 or 3 cm in diameter but it is usually very well

heard in the lung bases behind Patency of the ductus arteriosus particularly in infants may cause a moderate blowing pulmonary systolic murmur, not so intense as that of pulmonary stenosis and alone not to be interpreted as evidence of such patency A patent ductus arteriosus can be diagnosed by auscultation however only if there is a continuous humming top murmur Aneurysm of the aortic arch or descending aorta may cause rarely a systolic murmur in the pulmonary area as may also the occasional congenital coarctation of the aorta if well marked and the extremely rare true aneurysms of the pulmonary artery itself Finally systolic murmurs from other regions especially from the aortic area may be transmitted to the pulmonary area The fact that the very loud systolic murmurs and pronounced systolic thrills of both aortic stenosis and pulmonary stenosis are sometimes perceived almost equally well on both sides of the sternum or even best over the sternum itself makes the differentiation of these two conditions by auscultation alone at times difficult or even impossible the best differentiation by auscultation is by the transmission of the murmurs that of aortic stenosis being *widely and loudly* transmitted except to the lung bases where it is heard only faintly, and that of pulmonary stenosis being transmitted *not far* except to the lung bases

3 *Elsewhere over the precordium* There are two other areas besides apex and aortic and pulmonary areas where auscultation may reveal maximal sites for systolic murmurs They are at the lower end of the sternum and in the third and fourth intercostal spaces just to the left of the sternum Ruling out in the first place systolic murmurs transmitted from other areas where they are generally much louder we come to the very rare systolic murmurs originating in these two regions To the left of the sternum in the third or fourth intercostal space or in both a loud blowing systolic murmur may be heard in cases of congenital interventricular septal defect If such defect is uncomplicated (as is sometimes not the case) such a murmur is called the Roger murmur (and the condition Roger s disease) A palpable thrill usually accompanies this murmur Pulmonary or more probably infundibular stenosis is a less likely congenital cause for this type and position of murmur Finally a systolic murmur originating under the lower end of the sternum is rare signifying tricuspid regurgitation with a considerable degree of tricuspid stenosis Tricuspid regurgitation which is most often due to dilatation and not to valve damage is in contrast to mitral regurgitation rarely accompanied by murmurs probably because the tricuspid ring is larger and the right heart chamber pressure differences less Mitral regurgitation aortic stenosis or some congenital cardiac defect is by transmission much more likely than is tricuspid disease to cause a loud systolic murmur at the lower end of the sternum

4 *Vascular systolic murmurs* Murmurs systolic in time that is coincident with the appearance of the pulse wave are common over arteries At the base of the heart and in the main branches of the aorta three causes exist for their occurrence marked arterial dilatation with or without saccular aneurysms constriction by internal deformity or pressure from without (with the murmur

found at the end of the constriction where the caliber increases again to normal or beyond) and transmission of a loud murmur from the aortic area as in aortic stenosis Over the larger peripheral arteries like the brachial femoral, and popliteal pressure applied artificially from without easily produces systolic murmurs and thrills as is observed routinely in blood pressure studies Also compression by tumors cicatrices or other causes may give rise to systolic murmurs and thrills as may large aneurysms with active blood flow Over the veins isolated systolic murmurs are not found but as will later be mentioned continuous murmurs may be present Over the thyroid gland in exophthalmic goiter a very striking vascular murmur is heard called a bruit generally continuous with systolic accentuation and accompanied by a palpable thrill it is doubtless due to the greatly increased arteriovenous blood flow through the hyperactive gland

Systolic murmurs may be heard rather easily with either bell or Bowl s type of stethoscopic chest piece but as they rise in pitch they are more readily perceived by the Bowles receiver Certain murmurs are better brought out and are more likely to appear with the subject in one position than in another as for example the pulmonary systolic murmur which may be produced by the assumption of the supine position Finally one systolic murmur may be superimposed on another the harsher or louder one predominating making it very difficult to distinguish the two components

Diastolic murmurs Diastolic murmurs are less common but usually more important than systolic murmurs they have often been called the most serious auscultatory findings but this is not always so since the careful study of heart sounds and the detection and correct interpretation of certain frequent but neglected systolic murmurs may give us more information about the heart in the long run Diastolic murmurs are often difficult to hear It is for their detection that the use of the two stethoscopic chest pieces is so helpful and the examination of the subject in both upright and recumbent positions so important To test the effect of change in position it is most convenient and generally sufficient to examine the patient first upright and then supine or in the left lateral position Before proceeding with the special diastolic murmurs of intracardiac origin it should be noted that in diastole as in systole, though far less often respiratory murmurs may be produced by the action of the heart in squeezing air out of or sucking air into lung tissue especially if the lung happens to be fixed in close contact with the heart Such murmurs can be distinguished almost always by their respiratory quality by the ease with which they are caused to vary or disappear with forced respiration or change in body position by the fact that they tend to occur at an interval after the second heart sound and not directly with it frequently by their nearness to the ear and sometimes by the simultaneous occurrence of pulmonary rales due to the mechanical effect of the heart s action in sucking air in and out through moisture filled bronchioles It is quite likely that a few of these so called respiratory or other extracardiac diastolic murmurs are like systolic

murmurs produced by the friction of uninflamed pericardial or pleural surfaces (Ortiz 1933)

1 *At the apex* The only two diastolic murmurs heard at the apex with any degree of frequency are those due to mitral stenosis and to aortic regurgitation

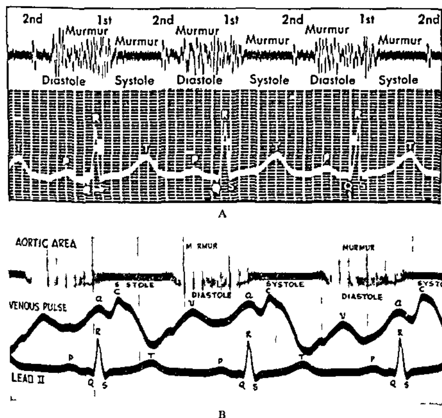


FIG 15 Phonocardiograms showing the diastolic murmurs of mitral stenosis and of aortic regurgitation (*A*) Stethoscopic electrocardiogram of a classical case of mitral stenosis with very rough mitral diastolic murmur sometimes with presystolic accentuation (note the first beat on the record) Slight systolic murmur also Observe the interval of relative silence between the second sound and the beginning of the middiastolic murmur of mitral stenosis in comparison with the absence of such an interval in the case of the aortic diastolic murmur in (*B*) (*B*) Logarithmic phonocardiogram *showing the very musical character of the high pitched aortic diastolic* murmur associated with retroversion of an aortic cusp Note that systole is clear Simultaneous venous pulse tracing and Lead 2 of the electrocardiogram are recorded (Kindness of Mr M A Rappaport Sanborn Company Cambridge)

These murmurs unlike superimposed systolic murmurs are so different that even when they occur together they can be differentiated

(a) *Organic mitral stenosis* The murmur of mitral stenosis (Figure 15A) has usually five characteristics that distinguish it from the murmur of aortic regurgitation (1) a rough rumbling character generally of low pitch and

sometimes so low as to be scarcely audible even to a trained ear (2) a failure to appear with or to follow immediately the second heart sound but instead an onset at a definite interval of time after the second sound that time interval being the ordinary interval between the second and third sounds of the heart, (3) a localization at the apex often over a small area of but 2 or 3 cm in diameter with no transmission beyond a characteristic that not infrequently causes the murmur to be missed entirely unless the examination is very careful and complete (4) a better perception by the employment of the bell chest piece of the stethoscope than by the employment of other types whose limited use may fail entirely to pick up the murmur when it is not loud and (5) a better perception with the patient recumbent the upright position sometimes failing to reveal the murmur even with the use of the bell receiver To these five characteristics may be added five others found less regularly but which are very useful in distinguishing the murmur (6) a palpable thrill localized closely as a rule over the apex in diastole usually somewhat shorter than the murmur (7) the presence in normal rhythm of a striking accentuation of the murmur in presystole just before or at the beginning of the first sound of the heart and due to the effect of atrial systole but absent if atrial fibrillation is present if the mitral stenosis is relatively slight or if the atrium is empty or weak when it contracts at the end of a prolonged diastole (8) the usual presence of an accentuated first heart sound at the apex so often characteristic of mitral stenosis (9) the common accentuation of the pulmonary second sound and (10) the frequent presence of a loud third heart sound at the left of the lower end of the sternum or in the space between this area and the apex and probably due to dilatation of the right ventricle

The murmur of mitral stenosis is explained by the vibration of heart walls and valve caused by the rush of blood through the stenosed mitral valve into the left ventricular cavity Its greatest intensity is usually at its onset at the time of the third sound when the flow of blood into the ventricle begins (which flow does not occur immediately at the time of the second sound when the aortic valves close at the end of systole) At the onset of the mitral diastolic murmur the flow of blood is as a rule faster than at other times because the intra atrial pressure with left atrium full of blood is greatest at such a time in relation to the low intraventricular pressure which in turn is caused by the passive elastic diastolic ventricular dilatation The force of the blood stream decreases as diastole proceeds and both murmur and thrill tend to fall off in intensity in diminuendo fashion to die away entirely if diastole is long (with atrium almost empty and ventricle full) or if the degree of the mitral stenosis is but slight If normal rhythm exists there is another increase in the speed of blood flow from atrium to ventricle in presystole due to atrial contraction If on account of a short diastole (fast heart rate) or marked valvular stenosis there is still a good deal of blood left in the atrium and still room for more in the ventricle the increase in blood flow through the stenosed mitral valve may be sufficient to cause a final accentuation variable in degree

and sometimes marked of the diastolic murmur and thrill just before the first sound or to make it audible again if it has entirely disappeared

The presystolic accentuation of the mitral diastolic murmur was formerly described as crescendo in character but the crescendo is actually an auditory illusion as shown by phonocardiograms and careful auscultation the illusion is due to the combined presence of a sudden accentuation of a murmur that has largely died away and the sharp first heart sound that terminates it This presystolic part of the murmur of mitral stenosis was at one time considered to be the whole murmur or at least the earliest to appear or the most important or characteristic part. But now we regard it as simply one part of the whole murmur at times striking to be sure but often absent as for example when there is atrial fibrillation (that is no orderly forceful atrial contraction) or too slight a degree of mitral stenosis to produce it If we would rely solely upon the presence of a presystolic murmur for a diagnosis of mitral stenosis we should miss at least half the cases of this valvular lesion Rarely may a presystolic murmur be present alone without a middiastolic murmur when the force and speed of blood flow through the stenosed valve happen to be greater in presystole than in middiastole and the degree of stenosis not sufficient to cause a murmur at both times Careful study of the case should however be made before recording a diagnosis of mitral stenosis on the basis of what appears to be a presystolic murmur alone without any diastolic rumble or murmur preceding it Marked accentuation and slurring of the first heart sound such as not infrequently occur in an overactive heart may give a semblance of a slight presystolic murmur and cause an erroneous diagnosis of mitral stenosis to be made when excitement exertion some nervous factor as in neurocirculatory asthenia or thyrotoxicosis is responsible If for any reason there is a suspicion of the possible presence of mitral stenosis because of rheumatic history sharp first sound loud third sound or unusual heart shape size or symptoms and no mitral diastolic murmur is present exercise (or the administration of a nitrite) may be used as a test to increase the rate of the heart and the speed of blood flow and to bring out a typical diastolic rumble at the apex Always it is best to examine the subject recumbent after such a test

Rarely the murmur of mitral stenosis may be a gentle and moderately high pitched blow following the third sound but almost invariably it is rumbling in nature and low pitched when the stenosis is pronounced An apical systolic murmur of mitral regurgitation may or may not be associated with the diastolic murmur of mitral stenosis The louder either one of these murmurs the less intense is the other and if either murmur is marked the other usually is absent

Cossio and Berconsky (1943) have pointed out the actual systolic rather than presystolic timing of the very brief vibrations (murmurs) that may precede the delayed and accentuated first heart sounds following the shorter diastolic pauses in atrial fibrillation in cases of mitral stenosis

(b) *Functional mitral stenosis* There is another fairly common cause of the mitral diastolic murmur besides actual organic mitral stenosis this is relative mitral stenosis due to considerable dilatation of the left ventricle with the valve normal or not sufficiently damaged to give rise alone to the obstructive diastolic murmur The clinical conditions in which such relative mitral stenosis is found are chiefly three namely moderate to severe acute or subacute rheumatic myocarditis high grades of anemia from any cause and well marked aortic regurgitation In a few scattered cases other causes of left ventricular dilatation are responsible such as congestive heart failure but as a rule cardiac dilatation associated with ordinary congestive failure is not attended by a mitral diastolic murmur in such cases there tends to be a third sound instead. Why this is so is not yet clear but it is probably because the blood flow is not fast enough in these hearts

In the case of aortic regurgitation various theories have been expressed as to the pathogenesis of the mitral diastolic murmur It has been generally thought that the blood stream regurgitating through the damaged aortic valve especially if the posterior cusp is involved or through the dilated aortic ostium impinges on the anterior cusp of the mitral valve thus forcing it back and producing a functional stenosis at a time in diastole when the blood stream is pouring from atrium into ventricle another theory suggests the production of the murmur by the contact of the two streams from aortic and mitral valves pouring together into the left ventricle with the anterior cusp of the mitral valve vibrating between them The best explanation however that fits not only the cases of aortic regurgitation but also the cases showing the characteristic murmur with no valve lesion at all is that the left ventricular dilatation is sufficient in degree to give rise to a murmur when the caliber of the blood stream coming through the normal mitral valve suddenly widens out The time relations quality location and other characteristics of this diastolic murmur of functional mitral stenosis are exactly the same as for organic mitral stenosis *except that there is as a rule less intensity to it and usually no associated palpable thrill* When the mitral diastolic murmur is found with aortic regurgitation without mitral stenosis it has been called the Austin Flint murmur (Flint 1862)

Flint Austin On Cardiac Murmurs *Am J M Sc* 1862 N S XLIV 29

Page 51 As a rule the force of the mitral direct current is not sufficient to develop a murmur unless there be mitral contraction Is this murmur ever produced without any mitral lesions? One would *a priori* suppose the answer to this question to be in the negative Clinical observation however shows that the question is to be answered in the affirmative I have met with two cases in which a well marked mitral direct murmur existed and after death in one of the cases no mitral lesions were found in the other case the lesion was insignificant I will proceed to give an account of these cases and then endeavor to explain the occurrence of the murmur

A mitral direct murmur then may exist without mitral contraction and with

out any mitral lesions provided there be aortic lesions involving considerable aortic regurgitation This murmur by no means accompanies aortic regurgitant lesions as a rule we meet with an aortic regurgitant murmur frequently when not accom panied by the mitral direct murmur The circumstances which may be required to develop functionally the latter murmur in addition to the murmur of aortic re gurgitation remain to be ascertained *Probably enlargement of the left ventricle is one condition* [Italics mine]

(c) *Transmitted murmurs* Other diastolic murmurs that may be heard at the apex are transmitted from elsewhere They are due to aortic regurgitation frequently to the very rare pulmonary regurgitation seldom and to tricuspid stenosis probably not at all the murmur in this last named condition not being distinguishable at the apex if it could be heard there from the murmur of mitral stenosis which is almost always much more prominent in such cases

2 *Diastolic murmurs at the base* In the case of basal diastolic murmurs the differentiation of sites is not so important as in the case of basal systolic murmurs since the two diastolic murmurs found are both heard maximally often in the same place and have the same characteristics Other data there fore than site and characteristics must generally be employed to differentiate them the most important point is that the murmur of aortic regurgitation is far more common than that of pulmonary regurgitation

(a) *Aortic regurgitation* (Figure 15B) The auscultatory characteristics that distinguish aortic regurgitation from mitral stenosis and tricuspid stenosis but not from pulmonary regurgitation are (1) a blowing rarely musical quality either high or low pitched often very gentle (2) an onset with or at once after the second heart sound the murmur if intense completely masking the sound (3) a maximal audibility over the midsternum and immediately to the left of it in the third and fourth intercostal spaces usually with wide trans mission to the apex and left axilla and upward less loudly toward the neck (4) a better perception with the Bowles type of stethoscopic chest piece than with the bell although rarely certain lower pitched aortic diastolic murmurs may be better heard with the bell or even with the naked ear and (5) a better perception as a rule with the patient upright and leaning forward than re cumbent In addition (6) a diastolic thrill is rarely felt accompanying this murmur (7) the murmur continues usually through all or most of diastole decreasing in intensity and never showing a presystolic accentuation (8) the first heart sound is not accentuated in fact frequently both heart sounds are masked by murmurs and (9) an accentuated third heart sound is not usually found Very often particularly if the diastolic murmur is marked there is also an aortic systolic murmur due either to aortic dilatation or to aortic valve stenosis but in the latter case as in mitral valve disease the louder one mur mur becomes the less loud is the other that is the greater the stenosis the less the regurgitation and vice versa It is common in aortic syphilis with aortic dilatation and regurgitation for both systolic and diastolic murmurs to be loud all over the cardiac area including the second intercostal space just to the right of the sternum with both heart sounds masked by them

The clinical conditions responsible for the aortic regurgitant diastolic murmur are firstly and much more frequently organic aortic valve disease due to rheumatic infection, syphilitic aortic involvement or sclerotic change and secondly dilatation of the aortic valve ostium without disease of the cusps themselves due occasionally to syphilitic aortitis and rarely to chronic hypertension sclerotic change senile ectasia, dissecting aortic aneurysm or severe anemia There is a very interesting variation of the aortic diastolic murmur more commonly found in syphilitic aortitis than in other conditions consisting of a very loud high pitched musical character with thrill and due apparently to eventration of one of the valve cusps (Bellet et al 1939 Nichol 1940) (see Figure 15B)

Uncommonly the aortic diastolic murmur is heard better in the aortic area that is in the second interspace just to the right of the sternum than it is along the left sternal border whither it generally is transmitted in maximal degree Such a maximal localization of the murmur in the aortic area is occasionally found in aortic regurgitation associated with marked aortic dilatation due to syphilitic aortitis when the ascending aorta extends further to the right and upward than normally or when along with the aortic valve the ascending aorta is displaced upward and to the right by a very large heart Also rarely the aortic diastolic murmur is heard better at the cardiac apex or at the lower end of sternum or between these sites than along the left border of the sternum if so it can easily be distinguished from the mitral (or tricuspid) diastolic murmur by its other characteristics described above Often the diastolic murmurs of aortic regurgitation and of organic or functional mitral stenosis occur together at the apex and can be readily distinguished Finally it should be stated that the diastolic murmur of aortic regurgitation may be found without any peripheral vascular signs this occurs in the lesser degrees of the valve defect if peripheral vascular signs like the water hammer or capillary pulse are awaited before aortic regurgitation is diagnosed half the cases of this valve lesion will be missed

(b) *Pulmonary regurgitation* Rare but almost exactly similar in its characteristics to the diastolic murmur of aortic regurgitation is that due to regurgitation through the pulmonary valve The resemblance may be so nearly complete that a distinction cannot be made by auscultation alone Rarely however does the pulmonary diastolic murmur ever reach in intensity the loudness frequently found in the case of the aortic diastolic murmur When it is unusually marked it is louder in the second left interspace (pulmonary valve area) than it is in the third and fourth interspaces and follows a markedly accentuated pulmonary second sound these are important clues In cases with well marked pulmonary diastolic murmurs there may also be other helpful signs namely abnormal visible or palpable pulsation in the pulmonary valve area a loud pulmonary systolic murmur water hammer pulsation in the pulmonary artery and 'dance of the lung hiluses seen by roentgen ray and abnormal right axis deviation by electrocardiogram Usually the pulmonary diastolic murmur is not transmitted so widely as is the aortic With a l

blowing diastolic murmur along the left sternal border well marked peripheral vascular signs such as the water hammer and capillary pulse are present if the murmur is due to aortic regurgitation and absent if it is due to pulmonary regurgitation this does not apply if the murmur is slight or moderate Percussion and roentgenologic and electrocardiographic studies are especially helpful in the differentiation between aortic and pulmonary regurgitation The clinical conditions underlying pulmonary regurgitation are most commonly (1) mitral stenosis causing increased pressure in the pulmonary circulation and dilatation of the pulmonary artery and valve ring without damage to the valve and rarely the remaining causes (2) chronic failure of the left ventricle with pulmonary vascular congestion and hypertension (3) chronic lung disease giving rise to the same mechanical conditions (4) chronic obliterating pulmonary endarteritis (5) congenital defect of the atrial septum with consequent flooding of the pulmonary circulation (6) congenital defect of the pulmonary valve giving rise to regurgitation (7) perhaps wide patency of the ductus arteriosus and (8) acute or chronic endocarditis of the pulmonary valve itself If mitral stenosis is the underlying clinical cause of the functional pulmonary regurgitation the diastolic murmur resulting is called the Graham Steell murmur (Steell 1881 1888)

Steell Graham *Physical Signs of Cardiac Disease* Edinburgh 1881 2nd ed page 43

Dr Balfour states that a diastolic murmur due to mitral stenosis may be audible and have its maximal intensity in the pulmonary area This murmur is soft and blowing unlike the apex true diastolic murmur of mitral stenosis and is probably produced in the pulmonary artery and infundibulum of the right ventricle as a murmur of high pressure the pulmonary artery being dilated and its valves permitting of a certain amount of regurgitation This murmur is not usually constant at least when first developed (See also *M Chronicle* Manchester December 1888 'The Murmur of High Pressure in the Pulmonary Artery)

3 *Elsewhere over the precordium* the diastolic murmurs heard are those already described transmitted there except for one very rare murmur heard maximally and often solely over the lower end of the sternum This exception is the diastolic murmur of *tricuspid stenosis* In every characteristic except that of position it is similar to the mitral diastolic murmur but it is usually less intense and may have more of a blowing nature In only extremely rare instances is it heard without an equally loud or louder mitral diastolic murmur and since sometimes the latter murmur is transmitted away from the apex and is heard at the lower end of the sternum a diagnosis of tricuspid stenosis by auscultation is rarely justified It may be suscepted if the typical diastolic murmur is louder over the lower end of the sternum than elsewhere over the precordium The presence of a palpable diastolic thrill localized at the same place or much more marked there than at the apex supports the diagnosis of tricuspid stenosis Other signs obtained by roentgen ray and general physical

examination are important The underlying clinical condition is organic tricuspid stenosis due to chronic rheumatic endocarditis

Functional tricuspid stenosis had not been described before I encountered several cases which I believed to be such with well localized mid diastolic murmurs near the lower end of the sternum mitral diastolic murmurs at the apex and loud pulmonary diastolic murmurs autopsy of one of the cases showed mitral stenosis obstructing thrombi in left atrium and pulmonary vessels and marked dilatation of pulmonary artery and right ventricle with no organic disease of pulmonary aortic or tricuspid valves This I reported in the third edition of this book in 1944 and have confirmed since

4 *Vascular diastolic murmurs* Vascular diastolic murmurs are rare Over the great vessels at the base of the heart there may be transmitted for a short distance a diastolic murmur originating in the heart, but this is far less common or marked than in the case of systolic murmurs Otherwise there is only the diastolic murmur produced in cases of aortic regurgitation or marked peripheral vasodilatation by the application of moderate to marked pressure over the larger arteries (best over femoral or brachial artery) First there appears the pistol shot sound and systolic murmur and then as the pressure is increased a slight to moderate blowing diastolic murmur is also heard (not a continuous murmur) The appearance of such a murmur is called Duroziez s sign (Duroziez 1861) The differentiation of the two causes of the murmur has been pointed out by Blumgart and Ernstene (1933) who showed that pressure with the distal and not proximal edge of the auscultatory bell will produce the murmur if aortic regurgitation is the factor responsible while the reverse is true in cases of peripheral vasodilatation in accord with the direction of blood flow and mechanism of murmur production discussed above

Continuous murmurs There is no continuous murmur of cardiac origin but there are three of vascular origin and all three of these may be heard over the region of the heart

1 Probably the most common and certainly the least important cause of such a continuous murmur is the mechanism giving rise to what has been called the *venous hum in the neck* with the subject seated or standing This murmur of humming character is loudest at the right side of the base of the neck and much less loud on the left side It is much increased by bending and turning the head to the left putting the blood vessels on the right side of the neck on the stretch It is easily and quickly obliterated by light pressure on the neck over the jugular veins sufficient to stop temporarily the downward flow of blood or by the assumption of the recumbent position—very simple pathognomonic tests It is a frequent finding in normal individuals especially children It is not evidence of any disease or pathologic state It is probably due to the rapid flow of blood (in the absence of all stasis) through the jugular veins into the jugular bulb and on into the superior vena cava Its importance so far as the heart is concerned is that it is frequently transmitted downward over the base of the heart even close to the lower end of the sternum and may give rise to such erroneous diagnoses as patency of the

ductus arteriosus and even aortic regurgitation if the diastolic phase of the hum happens to be prominent Such mistakes have been made in the past and since many physicians are unaware that there even exists such a phenomenon it behooves all examiners first to know that it does exist and then to exclude it before making a diagnosis of cardiovascular pathologic conditions Lian (1937) has also referred to the probability that rapid blood flow in the superior vena cava may be rarely responsible for a continuous murmur heard along the right sternal border

Brief mention should also be made of the umbilical venous hum heard in some cases of cirrhosis of the liver and in the case of certain congenital venous defects and called the Cruveilhier Baumgarten syndrome (Blain and Clapper 1945)

2 *Patency of the ductus arteriosus* A continuous murmur often with systolic accentuation heard best and sometimes only in the first or second interspace to the left of the sternum a little farther out than the site of the pulmonary systolic murmur and faintly or not at all in the neck is a characteristic sign of patency of the ductus arteriosus If patency of the ductus complicates congenital dextrocardia or a right aortic arch the continuous murmur is heard at the right border of the upper sternum This congenital defect may rarely occur however without murmurs or with but a slight to moderate systolic murmur in infancy or when the patent ductus is of very wide caliber If we can exclude the venous hum in the neck and arteriovenous aneurysms this typical mill wheel humming top machinery or tunnel murmur is pathognomonic of patency of the ductus arteriosus and can usually be confirmed by other findings The murmur may be transmitted to other parts of the precordium though usually it is not and it may be localized so high in the left side of the chest that it is missed on hasty or careless examination Its discovery is generally striking and may occasion undue alarm in the mind of an inexperienced examiner There may or may not be a continuous palpable thrill associated with it there usually is such a thrill if the murmur is intense

A very interesting new continuous murmur is that produced by the surgical treatment of the tetralogy of Fallot (see Chapter 13) here the subclavian (or innominate) pulmonary artery anastomosis produces a patent ductus like murmur on whichever side of the sternum the procedure is carried out

3 *Arteriovenous aneurysm* A continuous murmur usually with some accentuation in systole and attended by a thrill is found on auscultation over any direct arteriovenous connection sometimes called an arteriovenous aneurysm wherever it may be whether in the great vessels at the base of the heart (very rare occurrence) in the lungs in the head or neck or in the extremities (the most common site) Its interpretation is generally easy Such aneurysm is as a rule traumatic in origin by bullet shrapnel knife or even surgical accident (Linton and White 1945) it may be congenital (see Chapter 28)

Appearing abruptly at the left upper border of the sternum in a middle

aged or older individual with syphilitic aortitis a continuous murmur is to be interpreted as the result of rupture of aortic aneurysm into the pulmonary artery a very rare and serious event but one which may be compatible with some weeks or months of survival Correct antemortem diagnosis is possible even though the murmur exactly resembles that of patency of the ductus arteriosus

4 *Arterial aneurysm* A rare cause of a continuous murmur is an arterial aneurysm which may involve the aorta one of its major branches or a peripheral vessel usually over such a lesion if a murmur is heard at all it is only systolic in time but there are conditions such as wide open unthrombosed cavity with rapid blood flow when the murmur continues into diastole

5 *Coarctation of the aorta* Finally in some cases of congenital coarctation of the aorta a continuous murmur of slight to moderate intensity and not continuing throughout all diastole can be well heard over the thoracic spine

PERICARDIAL FRICTION RUB

Finally in cardiac auscultation we should observe the presence or absence of friction sounds due to acute pericarditis Such sounds vary from a soft almost blowing character to extremely rough loud rasping and leathery sounds Usually they are found in both systole and diastole and tend to be somewhat louder in systole They may occur in systole alone which fact adds to the difficulty of their differentiation from systolic murmurs The most common site is near the sternum especially along the left edge but they may be found anywhere or everywhere over the precordium and if loud enough they may be widely transmitted to the back and elsewhere If marked they are attended by palpable thrills It is often difficult in the presence of pericardial friction sounds to recognize the characteristics or even the existence of heart murmurs masked by them and if the friction sounds are of unusually soft character it may sometimes be difficult to distinguish them from murmurs Repeated and daily observations to note the variation and gradual increase or disappearance of such friction sounds may prove necessary for their interpretation and for the diagnosis of underlying valvular or other cardiac disease

Pericardial friction rubs are almost invariably indicative of acute pericarditis but there are occasional exceptions as pointed out by Ortiz (1933) when pericardial friction sounds or murmurs may be produced by normal pericardial surfaces rubbing against each other under unusual pressure particularly in the pulmonary valve area as in cases of pulmonary artery dilatation in thyrotoxicosis (Goodall 1920 Lerman and Means 1933) and of acute cor pulmonale due to pulmonary embolism (McGinn and White 1935)

BIBLIOGRAPHY

PHYSICAL EXAMINATION OF THE HEART

SEE ALSO REFERENCES UNDER GENERAL REFERENCES FOLLOWING CHAPTER 2

Inspection and Palpation

Dressler W *Die Brustwandpulsationen als Symptome von Herz und Gefasskrankheiten* Wilhelm Maudrich Wien 1933 Chapter 4

Pulsations of the Wall of the Chest" *Arch Int Med* 1937 LX 225 437 441 654 and 663

Cardiac Topography Pathologic Studies of the Anterior Aspect of the Heart and Its Relationship to the Anterior Wall of the Chest in Common Heart Diseases" *Am Heart J* 1940 XIX 141

Kellogg F and White P D "The Clinical Significance of Precordial Tenderness—The Relationship of Such Tenderness to Pain" *New England J Med* 1932 CCVI 659

Padilla, T Cossio P and del Castillo E B El latido toracico universal *Semana med* 1932 1 769

Percussion

Auenbrugger L *Inventum Novum ex Percussione Thoracis Humani ut Signo Abstrusos Interni Pectoris Morbos Detegendi* J T Trattner Vindobonae 1761 A facsimile of the first edition accompanied by the French translation of Corvisart the English translation by Forbes the German by Ungar and a biographical sketch by Dr Max Neuberger has been published by Josef Šafar Vienna and Leipzig 1922

Kurtz C M and White P D "The Percussion of the Heart Border and the Roentgen Ray Shadow of the Heart A Study of One Hundred Cases" *Am J M Sc* 1928 CLXXVI 181

Rotch T M "Absence of Resonance in the Fifth Right Interspace Diagnostic of Pericardial Effusion" *Boston M and S J* 1878 XCIX 389 421

Škoda J *Abhandlung uber Perkussion und Auskultation* L W Seidel Vienna 4th ed 1850 (1st ed 1839)

von Muller F "Aus dem Perkussionskurs" *Munchen med Wchnschr* 1928 CXXV 6 (Translation of this paper by R. W Buck in *New England J Med* 1928 CXCIX 807)

Auscultation Methods Sounds Gallop Rhythm

Batie E Sur la pathogénie du bruit de galop" *Progrès méd* 1880 VIII 593

Butterworth J S and Poindexter C A A Multiple Channel Electronic Stethoscope for Teaching and Demonstration *Am Heart J* 1948 XXXVI 112

Cossio P "Choque de la punta mitral" *Rev Argentina de Cardiol* 1943 X 145

Einthoven W and Geluk M A J "Die Registrirung der Herztone" *Pflugers Arch f d ges Physiol* 1894 LVII 617

Huchard, H "Contribution à l etude clinique des tendons aberrants du coeur *Rev de méd* 1893 XIII 113

Kerr W J Althausen T L Bassett A M and Goldman M J "The Symballophone A Modified Stethoscope for the Lateralization and Comparison of Sounds *Am Heart J* 1937 XIV 594

Laennec R T H *De l auscultation médiate ou traité du diagnostic des maladies des poumons et du coeur fondé principalement sur ce nouveau moyen d'exploration* Brosson et Chaude Paris 2nd ed 1826 (1st ed 1819)

Levine S A., and Harvey W P *Clinical Auscultation of the Heart* W B Saunders Co Philadelphia 1949

Lian, C., and Dang Van-Chung "L auscultation dorsale des souffles et frottements dans les affections cardiovasculaires *Presse méd* 1950 LVIII 585

Lian C and Goeblin V Les bruits du coeur foetal in utero (Étude phonocardiographique) *Arch d mal d coeur* 1938 XXXI 173
Luisada A Variable Interval between Electric and Acoustic Phenomena in Auricular Fibrillation *Am Heart J* 1941 XXII 245
Mannheimer E *Calibrated Phonocardiography and Electrocardiography A Clinical Statistical Study of Normal Children and Children with Congenital Heart Disease* Acta Paediatrica 1940 XXVIII Suppl II
Calibrated Phonocardiography *Am Heart J* 1941 XXI 151
Rappaport M B and Sprague H B "Physiologic and Physical Laws that Govern Auscultation and Their Clinical Application The Acoustic Stethoscope and the Electrical Amplifying Stethoscope and Stethograph *Am Heart J* 1941 XXI 257
"The Graphic Registration of the Normal Heart Sounds *Am Heart J* 1942 XXIII 591
Thayer W S On the Early Diastolic Heart Sound (the So Called Third Heart Sound) *Boston M and S J* 1908 CLVIII 713
White P D "The Clinical Significance of Gallop Rhythm *Arch Int Med* 1928 XLI 1

Murmurs and Pericardial Friction Rub

Bellet S Gouley B Nichols C F and McMillan T M "Loud Musical Diastolic Murmurs of Aortic Insufficiency *Am Heart J* 1939 XVIII 483
Blain A III and Clapper M "The Cruveilhier Baumgarten Syndrome" *New England J Med* 1945 CCXXXII 647
Bland E F White P D and Jones T D The Development of Mitral Stenosis in Young People with a Discussion of the Frequent Misinterpretation of a Middiastolic Murmur at the Cardiac Apex *Am Heart J* 1935 X 995
Bloom H J G Venous Hums in Hepatic Cirrhosis *Brit Heart J* 1950 XII 343
Blumgart H L and Ernstene A C Two Mechanisms in the Production of Duroziez Sign Their Diagnostic Significance and a Clinical Test for Differentiating between Them *J A M A* 1933 C 173
Cossio P and Berconsky I "El primer ruido cardiaco y el soplo presistolico en la estrechez mitral con fibrilación auricular *Rev Argentina d Cardiologia* 1943 X, 162
Duroziez P Du double souffle intermittent crural comme signe de l insuffisance aortique *Arch gén de med* Paris 1861 I 417 588
Flint A On Cardiac Murmurs *Am J M Sc* 1862 XLIV 29
"The Mitral Cardiac Murmurs *Am J M Sc* 1886 N S XCI 27
Goodall J S "The Heart in Graves Disease *Practitioner* 1920 CV 37
Kerr W J Harp V C Rapaport E and Bierman H R The Propagation of Murmurs and the Local Production of Vascular Murmurs in Relation to the Pulse Waves *Tr A Am Physicians* 1948 LXI 308
Landis H R M and Kaufman I "The Occurrence of Venous Hums in Children *Arch Pediat* 1912 XXIX 88
Lerman J and Means J H "Cardiovascular Symptomatology in Exophthalmic Goiter" *Am Heart J* 1933 VIII 55
Levine S A "The Systolic Murmur *J A M A* 1933 CI 436
Lian C Le souffle continu du cave supérieur *Bull et mém d l soc méd d hop d Paris* 1937 LIII 1088
Linton R R and White P D "Arteriovenous Fistula between Right Common Iliac Artery and Inferior Vena Cava Report of Case of Its Occurrence Following Operation for Ruptured Intervertebral Disk with Cure by Operation" *Arch Surg* 1945 L 6
McGinn S and White P D "Acute Cor Pulmonale Resulting from Pulmonary Embolism Its Clinical Recognition" *J A M A* 1935 CIV 1473
Master A M "Apical Systolic Murmur" *Arch Int Med* 1948 LXXXI 518
Nichols C "A Study of Syphilis of the Aorta and Aortic Valve Area *Ann Int Med* 1940 XIV 960
Ortiz R T "Una nueva teoria de los soplos anorgánicos frotamientos cardiaseroses *Arch Lat Am d Cardiol y Hematol* 1933 III 45

Rivero Carvallo J M Carral R and Ramirez Jaime M H Estenosis relativa de la tricuspide *Arch del Inst de cardiol Mexico* 1951 XXI 47
Roger H Recherches cliniques sur la communication congenitale des deux coeurs par inocclusion du septum interventriculaire *Bull d l Acad d med d Paris* 1879 VIII 1074
Rogers O H and Hunter A Heart Murmurs and Their Influence on Longevity *Proc 30th Annual Meeting As Life Ins M Dir America* 1920 VI 173
Steell Graham "The Murmur of High Pressure in the Pulmonary Artery *M Chronicle* Manchester 1888 IX 182
Wells B G Rappaport M B and Sprague H B 'The Graphic Registration of Basal Diastolic Murmurs" *Am Heart J* 1949 XXXVII 586
White P D Adams F D and Craib D Note on Cardiac Murmurs Recommendation for a Revised Terminology *Am J M Sc* 1942 CCIII 52

CHAPTER 6

SPHYGMOMANOMETRY NORMAL AND ABNORMAL BLOOD PRESSURE

Hales S *Statistical Essays Containing Haemostaticks or an Account of some Hydraulic and Hydrostatical Experiments Made on the Blood and Blood Vessels of Animals* W Innys and R Manby London 1733 Vol 2

Page 1 1 In *December* I caused a Mare to be tied down alive on her Back she was fourteen Hands high and about fourteen Years of Age had a Fistula on her Withers was neither very lean nor yet lusty Having laid open the left crural Artery about three Inches from her Belly I inserted into it a brass Pipe whose Bore was one sixth of an Inch in Diameter and to that by means of another brass Pipe which was fitly adapted to it I fixed a glass Tube of nearly the same Diameter which was nine Feet in Length Then untying the Ligature on the Artery the *Blood* rose in the Tube eight Feet three Inches perpendicular above the Level of the left Ventricle of the heart But it did not attain to its full Height at once rushed up about half way in an Instant and afterwards gradually at each Pulse twelve eight six four two and sometimes *one Inch When it was at its full Height it* would rise and fall at and after each Pulse two three or four Inches and sometimes it would fall twelve or fourteen Inches and have there for a time the same Vibrations up and down at and after each Pulse as it had when it was at its full Height to which it would rise again after forty or fifty Pulses

Hales pioneered in the estimation of venous pressure also On page 13 he wrote as follows

1 In *December* I laid a common Field Gate on the Ground with some Straw upon it on which a white Mare was cast on her right side and in that Posture *bound fast to the Gate* she was *fourteen* Hands and three Inches high lean tho not to a great Degree and about ten or twelve years old This and the above mentioned Horse and Mare were to have been killed as being unfit for service

"2 Then laying open the left Jugular Vein I fixed to that part of it which comes from the Head a glass Tube which was four Feet, and two Inches long

"3 The Blood rose in it in three or four Seconds of Time about a Foot, and then was stationary for two or three Seconds then in three or four Seconds more it rose sometimes gradually and sometimes with an unequally accelerated motion

nine Inches more on small Strainings of the Mare Then upon greater Strainings it rose about a Yard and would subside five or six Inches

Sphygmomanometry (σφυγμος pulsation μαιος thin or rare—rarity or tension—and μετρον measure) consists of measurement of the arterial blood pressure It is a special method of cardiovascular study which through its introduction as a routine part of physical examination during the past generation has revealed the cause of much cardiac enlargement and failure that was previously obscure

Two centuries or more ago and again one hundred years later actual determinations of the blood pressure of animals were made by the insertion of tubes into arteries to measure the height first to which the blood column ascended (Hales 1733) and second to which it forced a mercury column (Poiseuille 1828) but the study was applied only to animals in experimental work until much later However long before the development of a satisfactory clinical sphygmomanometer rough attempts were made to estimate human blood pressure by measuring the weight or force needed when attached to a sphygmograph to obliterate the radial pulse (Vierordt 1855) There followed gradually the methods of pressure application by plethysmograph to the hand (Marey 1876) later by pelottes to the radial artery (von Basch 1881) and then to the brachial artery and finally by small and then larger fluid filled cuffs applied to finger or arm (Riva Rocci 1891) At last came the introduction of the present comfortable wide air filled cuffs for application to the upper arm and to the leg

Arterial blood pressure in man is read off for convenience in millimeters of mercury instead of in centimeters of water (which would require a measuring tube over 13 times longer) The gauge is either a carefully graduated and calibrated tube of mercury or a spring pressure device with dial and needle (von Basch 1887) There are today many different models and makes of sphygmomanometers some of these are more convenient more accurate or better made than others but most of them are satisfactory provided they are checked for accuracy Errors may creep into the use of any type of sphygmomanometer too airtight a seal of a tube containing a mercury column may for example by air compression or by relative vacuum result in errors in blood pressure readings too low during inflation of the cuff and too high during decompression completely to nullify the generally reputed greater accuracy of the mercurial sphygmomanometer A maximal error of 3 mm of mercury may be considered permissible for sphygmomanometers in routine clinical use at pressures up to 300 mm of mercury the average error should be considerably less but great accuracy is not needed clinically since the significance of variations of a few millimeters of blood pressure is generally negligible

Special sphygmomanometers have been devised for special purposes such as the recording sphygmomanometers which take graphic records of value

where objective data are desired for a permanent file and the oscillometer which shows at different pressure levels the fullness of the pulse in a quantitative way The latter is especially useful in studying the peripheral circulation when there is vascular disease or obstruction A useful new instrument introduced to register the blood pressure in the pulmonary artery and its branches the right ventricle the right atrium and the great veins during cardiac catheterization is an electromanometer devised especially for this purpose superseding the Hamilton manometer There are various instruments and methods for the study of the venous blood pressure dependent on (1) the force applied by a pelotte (with manometer) to stop the venous flow (2) the amount of air pressure under a glass capsule measured in centimeters of water necessary to cause collapse of a vein of moderate size usually on the back of the hand or forearm (von Recklinghausen 1906 Hooker and Eyster 1908) (3) the height above the level of the right atrium in centimeters to which the forearm and hand are raised before the veins collapse (Frey 1902 Gaertner 1903) and the most satisfactory method (4) the direct reading of the pressure in centimeters of blood or of sterile normal salt solution in manometer tube connected with a needle introduced into an elbow vein at the level of the right atrium (Moritz and Tabora 1910 Griffith et al 1934 Holt 1940) A method for the graphic registration of the venous blood pressure has also been devised (Kendrew 1926) Finally methods for determining the capillary blood pressure have been introduced including (1) macroscopic blanching of the skin by pressure under a transparent capsule a method which is unsatisfactory because it includes the pressure in the smaller arterioles and venules as well (2) the more accurate microscopic method of direct observation of the blood flow in the capillaries (Lombard 1912) and most accurate of all (3) direct registration of pressure by the introduction of a fine pipette into a capillary (Landis 1930, Eichna and Bordley 1939)

The systemic blood pressure cannot be estimated by palpation alone with enough accuracy to warrant any confidence in such a procedure Instrumental sphygmomanometry is essential There are three technics which as a matter of fact may be combined for the sake of greater accuracy

The best method of clinical sphygmomanometry is the *auscultation* technic which records systolic and diastolic pressures in most cases very slightly below the actual levels as determined by direct readings from within the artery The systolic pressure is to be read at the point when the first clear sound appears during slow decompression of the blood pressure cuff faint sounds due to the impact of a forceful pulsation against the closed end of the artery at the upper edge of the cuff may sometimes be transmitted to the stethoscope placed over the artery at or just below the lower edge of the cuff at any pressure above the systolic but these should be ignored The diastolic pressure should be recorded at the point when the sound abruptly disappears or abruptly drops in intensity rarely the sound continues loudly to zero and the diastolic pressure must be so recorded as in some cases of marked aortic

regurgitation In 1939 a joint report was published by committees appointed by the American Heart Association and by the Cardiac Society of Great Britain and Ireland for the standardization of blood pressure readings in which there appeared a note of difference of opinion relative to a record of the diastolic pressure the American committee recommended that both the level at which the auscultatory sounds become dulled and that at which they disappear (if there is a difference) should be recorded thus 140/80 70 or 140/70 0 or 140/70-70 while the British committee believed that except in aortic regurgitation it is nearly always possible to decide the point at which the change comes (either abrupt dulling or complete disappearance) and that this is the only reading that should be recorded A report by a new committee of the American Heart Association in 1951 states that it appears that the point of complete cessation is the best index of diastolic pressure

There is no practical value in attempting to record the various auscultatory phases of the pulse pressure that is in the interval between the systolic and diastolic levels except in one respect to be recounted below usually the upper most phase is one of sound the second phase which lasts normally over an interval of about 20 or 30 mm of mercury is one of murmur the third phase is one of sound again and occasionally there is a short fourth phase of dimin ished sound before the level of silence is reached below the diastolic pressure The one auscultatory phase that is of special importance and of practical interest is that related to the so called *auscultatory gap* In occasional cases the murmur phase may be largely or wholly absent leaving a gap of absolute or relative silence in the middle or upper part of the pulse pressure range Such a finding is most frequent in chronic hypertension aortic stenosis and marked local arteriosclerosis its exact mechanism is not clear An example of such an auscultatory gap is one of 35 mm ranging from 180 to 145 in a patient with systolic pressure of 210 and diastolic of 105 To avoid an im- portant error in such a patient it is necessary to raise the compression of the cuff far enough above this gap so that the true systolic sounds can be heard on decompression or to check the method by either or both of the other two methods of sphygmomanometry one can easily carry out both these pro cedures If the auscultatory gap is not recognized there may be recorded a systolic pressure as much as 50 mm or more below what it actually is There are still other sources of error in auscultatory sphygmomanometry too low a reading when the arm is especially small and too high when the arm is very large but these errors are not great (Bordley and Ragan 1941) and in general the method is an unusually accurate bedside procedure as checked by direct intra arterial readings (Steele 1942)

A second method of sphygmomanometry the *oscillatory* is theoretically more accurate than the other technics but actually less practical because of the frequent difficulty in making the readings The systolic pressure is the point of abrupt increase in amplitude of the oscillations of the mercury column or needle of the manometer above the baseline of small pulse move ments while the diastolic pressure is the first point of distinct decrease below

the maximal oscillations unfortunately however both these points may be poorly marked because of the failure of any abrupt changes The method may be carried out visually or by a recording device (Figure 16) Its greatest value is its service as a check on the accuracy of the more practical auscultatory method except in the study of obstructive arterial disease in the extremities when it has been found that the form of the oscillographic curve is of some importance in determining variations from the normal in the vascular tree and apparently in determining the type of arteriosclerosis (Friedlander 1935)

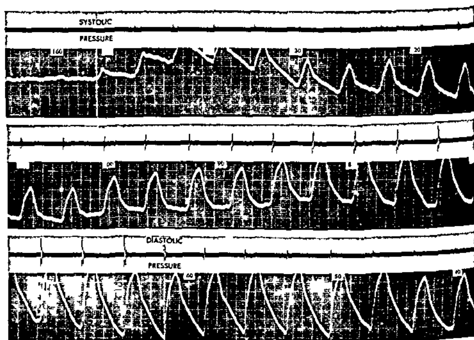


FIG 16 Human arterial blood pressure record determined by simultaneous brachial arterial tracing and phonogram at systolic pressure of 150 and diastolic pressure of 62 The first definite upstroke of the arteriogram occurs just prior to the record of the first sound The disappearance of the truncated dip of the arterial tracing occurs at the time of the last well marked sound record (Kindness of Mr M A Rappaport Sanborn Company Cambridge)

The third method of sphygmomanometry is *palpatory* The point at which the radial pulse is first felt on decompression of the brachial cuff is recorded as the systolic pressure but this is invariably too low by about 5 to 10 mm The method serves however as a rough check on the other methods outlined above The diastolic pressure cannot easily be recorded by palpation and this explains why in the early days of sphygmomanometry only the systolic blood pressure was measured Segall however a decade ago (1940) called attention to the possibility of palpating over the brachial artery the vibrations set up during the pulse pressure interval which correspond to the sounds and murmurs heard by the auscultatory method between systole and diastole

It is of academic interest that the subject himself can roughly note the levels of systolic and diastolic blood pressure in the arm by the sensations during decompression of the cuff a thrill is felt subjectively just below the systolic pressure level and disappears just above the diastolic level

Finally there has been a revival for certain special studies of the old time direct arterial blood pressure by arterial puncture in man (Wolf and Kindler 1934) and there have been introduced in recent years methods of recording by cardiac catheterization the actual pressures in right atrium right ventricle and pulmonary artery and its branches an especially important development (Cournand et al 1944 Dexter et al 1947)

Systemic arterial blood pressure The blood pressure in the brachial artery of a normal adult ranges from 95 to 145 mm of mercury *systolic* depending on conditions at the time of the sphygmomanometry Age has some effect on blood pressure as recently confirmed by Master (1950) There tends to be an increase though often irregular in systolic pressure of ½ to 1 mm a year Thus at twenty years the systolic blood pressure normally may be 110 mm at thirty in the same person 115 at sixty 150 and so on Factors of excitement exercise eating smoking and fatigue all play a considerable role in many persons tending to elevate the systolic blood pressure moderately Nervous tension is the factor that influences blood pressure most elevating it in both normal and hypertensive individuals but especially in the latter Ayman and Goldshine (1940) found for example that in a series of hypertensive individuals 30 per cent registered a systolic pressure 40 mm or more higher in the clinic than at home and 24 per cent a diastolic pressure 20 mm or more higher The temporary hypertension that is found in many nervous but otherwise normal young men at the time of examination for athletic sports military service or insurance is well known in fact it is so common that routine blood pressure determination for admission to the army was at one time even considered inadvisable Figure 17 illustrates the wide range of the normal brachial blood pressure

The pressure varies also slightly with the respiratory phase but this is unimportant unless the respiration is greatly disturbed or the heart constricted by acute or chronic pericarditis when the pulse may become markedly *paradoxical* (see Chapter 27) the paradoxical pulse consists of marked decrease of the systolic and pulse pressures even to the point of obliteration during inspiration in contrast to the usual and normal increase of the pulse during inspiration in the case of diaphragmatic breathing

In the early morning before arising the systolic brachial arterial pressure may be 105 mm while in the same person in the midst of a busy day it may register as much as 140 strenuous exercise may send it up to nearly 200

The most important and commonest cause of abnormal high systolic blood pressure is hyperpiesia (essential or arterial hypertension) less common causes are nephritis obstruction to the renal circulation (Goldblatt 1934) convulsive seizures brain tumor tumor of the adrenal medulla (pheochromocytoma) and coarctation of the aorta (see Chapter 19) The causes of ab

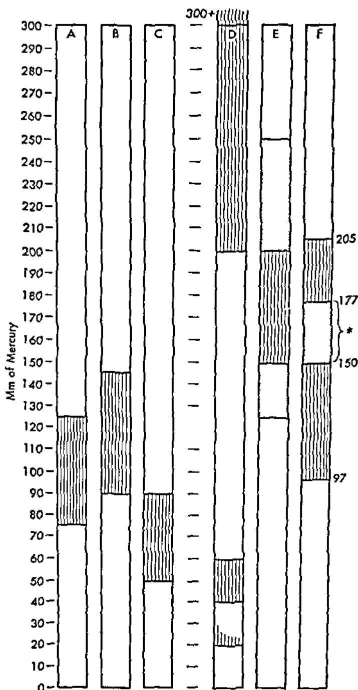


FIG 17 Diagram showing (*A*) the average normal adult blood pressure (1?5 ı mercury systolic and 75 diastolic) (*B*) the usual upper limits of normal pressure (the lower limits of normal pressure (*D*) the extreme upper range of pressure v hypertension and an extreme lower range of pressure with hypotension the diast pressure in aortic regurgitation may drop almost to 0 (broken lines) (*E*) the va bility of the systolic pressure (from 250 to 200) and of the diastolic pressure (fr 150 to 125) possible over an interval of 10 minutes in a given case of hyperpie

normally low systolic blood pressure are vasomotor or vascular shock Addison s disease and to a lesser degree acute and chronic constrictive pericarditis and aortic stenosis

The *diastolic* arterial blood pressure range is normally much less than the systolic a low reading in an adult is 60 mm of mercury and a high 90 It records the basic pressure in the circulatory system and so is fundamentally more important than the systolic pressure which is but very transient at its full height

The causes of abnormal increase of the diastolic blood pressure are the same as those recorded above for the systolic pressure The causes of abnormal decrease of the diastolic pressure are the same as for decrease of systolic pressure and in addition aortic regurgitation

In late years particularly in France much interest has been expressed in the so-called *average dynamic* or *mean effective* blood pressure which is the total pressure leveled off from the peaks and hollows of systolic and diastolic pressures *that is such a pressure as would assure during a certain interval* of time a steady flow of the same amount of blood as passes through a given vessel under the variations of pressure ordinarily found with each heart cycle This mean effective or average dynamic blood pressure gives to be sure a clearer idea than any other reading of the total pressure strain on the circulation but it has the defects of not taking into account the swing of the pulse pressure which is important and of being difficult to estimate accurately although Vaquez and his associates (1932 and 1933) thought that the maximal oscillation of the pulse excursion just above the diastolic level in sphygmomanometry represents with sufficient accuracy the mean pressure Moreover the mean pressure is usually close to and parallel with the diastolic blood pressure the level of which may be used as an adequate guide along with the pulse pressure Wiggers (1942) called attention again to the mean pressure but emphasized rather the importance of the pulse pressure

The *pulse pressure* is the difference between the systolic and diastolic pressures normally ranging in an adult at rest from 40 mm (for example with systolic pressure of 120 and diastolic of 80) to 70 (for example with systolic pressure of 140 and diastolic of 70)

An abnormal increase of pulse pressure is most commonly due either to an especially high systolic pressure in systemic hypertension (pulse pressure of 120 mm for example with systolic pressure of 220 and diastolic of 100) or to a low diastolic pressure in aortic regurgitation or marked peripheral vasodilatation (pulse pressure of 110 mm for example with systolic pressure of 140 and diastolic of 30) An abnormal decrease of pulse pressure is most commonly found in states of vasomotor shock with or without syncope (15 mm for example with systolic pressure of 65 and diastolic of 50) aortic steno-

and (*F*) auscultatory gap averaged in a series of 30 cases showing this phenomenon (26 with hyperpiesia 2 with hyperpiesia and aortic stenosis and 2 cases of aortic stenosis without hypertension 205 mm = average systolic pressure 97 mm = average diastolic pressure and * = average auscultatory gap ranging from 177 to 150 mm)

sis (25 mm for example, with systolic pressure of 110 and diastolic of 85 acute or chronic constrictive pericarditis (20 mm for example with systol pressure of 105 and diastolic of 85) or adrenal insufficiency in Addison's disease (20 mm for example with systolic pressure of 80 and diastolic of 60)

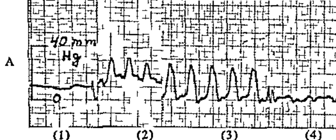
A very abnormal and clinically significant variation of pulse pressure is an alternation found when the heart rhythm is regular or after premature beats (extrasystoles) and due chiefly to a fall in systolic pressure of a few milli meters (2 or 3 to 20) every other beat this is the *pulsus alternans* a sign of serious weakness and probably of alternating strength of contraction of the left ventricle when the pulse is not excessively fast (see Chapters 8 and 30)

The blood pressure in children is less than in adults beginning at about 65 systolic and 40 diastolic in earliest infancy and rising slowly to the adult levels soon after adolescence

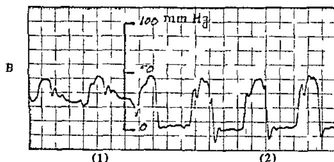
Finally it is important to note that the usual blood pressure readings refer to the pressure in the brachial artery on one side It is often wise to measure the blood pressure in both arms (especially if there is suspicion of syphilitic aortitis) and to repeat blood pressure measurements several times at inter vals of a few minutes if abnormal readings are found at first The pressure in other arteries of the body varies according to their size position and state of contraction Thus the blood pressure in the aorta is normally greater than that in the brachial artery while that in a digital artery is considerably less The pressure in the femoral artery is greater than that in the brachial artery for four reasons (1) its larger size (2) the greater bulk of soft tissue mass to be compressed in the leg (3) the lower position of the femoral artery in the body in the upright position hydrostatic pressure thus adding its effect, and (4) a certain amount of compensatory vasoconstriction in the lower part of the body in the erect posture Localized vasoconstriction may occur still further to vary the pressures and sometimes exposure of a part of the body (the arm for example) to cold causes a general vasoconstriction excessive in hypertensive cases and perhaps in potential hypertensive cases (see Chap ter 31) Hardness of the arterial wall affects little or not at all the blood pressure readings made by the various indirect methods (Dameshek and Loman 1932 Ayman and Krakower 1933) although loss of elasticity of the walls of the larger arteries favors a larger pulse pressure The act of compression of the arm may itself reflexly affect the first blood pressure levels and not simply from apprehension so that several readings are some times necessary I find that it is best for this very reason to inflate the cuff at first only a little above the diastolic pressure and to record that reading during decompression before inflating to a much higher pressure to obtain the systolic reading especially in hypertensive patients

Pulmonary arterial blood pressure During the past few years one of the most desired and needed advances in human physiology has come to pass namely the measuring and recording of the blood pressure in the pulmonary circulation by means of cardiac catheterization and electrical or optical ma nometer (Dexter et al 1947) (see Figure 18) In fetal life the pulmonary

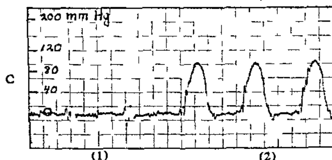
A



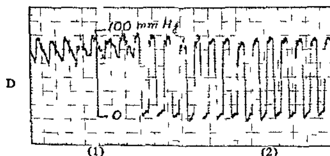
B



C



D



18 Blood *pressure by cardiac catheterization* (*Kindness of Dr Gordon S Myers* Massachusetts General Hospital Boston)

In a normal 36 year-old man
1 Standardization in millimeters of mer ury
2 Pulmonary artery pressure
3 Right ventricular pressure
4 Right atrial pressure

In a 24 year-old woman with mitral stenosis
1 Pulmonary artery pressure
2 Right ventricular pressure

C In a 19 year-old female with pure pul monary stenosis of high degree
1 Pulmonary artery pressure—ab normally low with feeble pulsations
2 Right ventricular pressure—very high

D In a 3 year-old girl with tetralogy of Fallot
1 Tip of catheter overriding aorta
2 Pressure in right ventricle

circulation is minimal *but the right ventricle maintains through* the paten ductus arteriosus the major part of the systemic circulation and is larger than the left ventricle Soon after birth when the ductus arteriosus closes the pressures of pulmonary and systemic circuits are undoubtedly very nearly equal, hence at birth it may be said that the pulmonary blood pressur probably measures about 50 to 60 mm of mercury since that *is the system* blood pressure at this time Normally the right ventricle fails after birth to maintain the systemic circulation and therefore the pulmonary blood pressur quickly falls below the level of the systemic pressure since the short rapidl dividing pulmonary arterial tree produces relatively little resistance In th human adult the systolic blood pressure in the main pulmonary artery meas ures normally 15 to 35 mm of mercury with average of 25 mm (Figure 18 and the diastolic pressure is about 10 mm of mercury On the other hand when the pulmonary circulatory resistance is much increased as in high grad mitral stenosis left ventricular failure pulmonary endarteritis or sever chronic pulmonary disease the pulmonary arterial pressure rises considerab and may even surpass the systemic arterial pressure as further indicated b the fact that in some cases the right ventricle actually exceeds the left ventric in size and weight A rough check on the relationship between but not th actual levels of the systemic and pulmonary arterial pressures can be ma by comparing the intensities of the aortic and pulmonary second *heart sound*

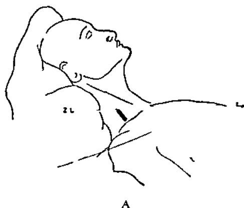
Periodic variations of pulmonary blood pressure of considerable exte have been found to occur in experimental animals and also in man wi respiration Both systolic and diastolic pressures fall with inspiration an rise with expiration the systolic more than the diastolic Also during cycles apnea and hyperpnea the pulmonary blood pressure varies *the systolic pre* sure falling and the diastolic rising during apnea

Intracardiac blood pressure It has become possible since the publicatio of the third edition of this book to measure accurately and to record in m the blood pressures in the right heart chambers by intracardiac catheterizatio (*Cournand et al 1944*) and the use of a manometer (*Hamilton*) *or a mo* recently devised electromanometer (Figure 18) Normally in the huma adult the right atrial pressure under as basal conditions as can be attaine measures from +2 or +3 to −2 or −3 mm of mercury averaging 0 mm an the right ventricular pressure ranges from +15 to +35 systolic and from *to +2 mm diastolic The pressure in the left heart chambers is* as yet n determinable normally but the left atrial pressure has been measured direct in the case of a congenital atrial septal defect being about +5 to +10 m of mercury therewith and at operation in mitral stenosis being found measure about +30 mm varying with the degree of valvular obstruction

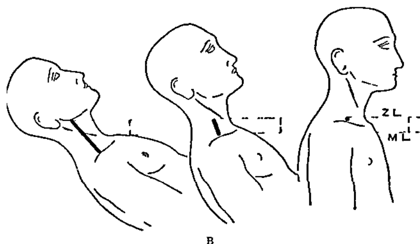
Venous blood pressure The venous blood pressure was measured two hun dred years ago by Hales who inserted a manometer directly into the jugul vein of a mare (Hales 1733)—see quotation at the beginning of this chapte The venous blood pressure may be measured with a fair degree of accurac as has been shown by ascertaining the actual pressure level vertically abo

:vel of the junction of the superior vena cava and the right atrium (ap- mately one third the distance through the chest from front to back at ower border of the third right sternocostochondral junction) to which l will rise or displace normal salt solution in a tube connected by trocar :edle with an arm vein (Moritz and von Tabora 1910 Holt 1940) ore conveniently by a spring phlebomanometer connected with the vein ch and Winsor 1943) In logical evolution from these cruder technics ewest and most accurate though not exactly routine method of venous l pressure measurement is by intravenous catheter and special electro- ometer

simple but generally adequate clinical method of determining the



A



B

IG 19 The level of the height of the blood column in the jugular vein (*A*) In ormal person recumbent (*B*) In a person with increased systemic venous pressure lifferent inclinations of the body Z.L = zero level M L. = manubrial line (Lewis, *Diseases of the Hea t* 4th ed The Macmillan Company New York 1946)

venous pressure requiring no apparatus except a centimeter scale is to measure the height above the lower border of the third costal cartilage at the right border of the sternum (level of mouth of the superior vena cava) to which the blood rises in the jugular vein with the subject sitting upright if the pressure is within the normal range that is below 10 cm the vein will not be evident and if it is very high that is above 25 cm the blood column will rise out of sight under the ear slight to moderate elevations can be readily measured (Figure 19) A third but now outmoded method is by determining the amount of air pressure (best measured in centimeters of water) necessary to collapse a superficial vein of moderate size in forearm or hand An apparatus for making such a measurement has already been mentioned (page 110) Obesity thick skin or sclerosis of the veins may make such determination difficult

The normal venous pressure varies widely from 4 to 10 cm of water (about 1½ to 6 mm of mercury) Usually it amounts to about 6 to 7 cm of water being about one half in millimeters of water of the normal arterial pressure in millimeters of mercury and therefore about 1/20 of the arterial pressure The systemic blood pressure thus drops from say 130 to 5 mm of mercury as it progresses from brachial artery through its branches and through arterioles capillaries and venules to a superficial vein of moderate size on the back of the hand or on the forearm If the venous pressure by the usual method measures 10 cm or more of water it is abnormally high Exercise may temporarily raise the pressure considerably even as high as 20 cm of water but the three conditions which are associated with abnormally high venous pressure at rest, even to 30 cm of water or more are congestive heart failure of considerable or moderate degree acute or chronic constrictive pericarditis and venous obstruction due to thrombosis or compression If the right ventricle remains competent while the left ventricle has failed there is pulmonary congestion and increased pulmonary venous pressure due to left ventricular weakness even though the systemic venous pressure remains normal

A very interesting phenomenon is encountered in some cases with well marked tricuspid regurgitation without much constant distention of the systemic veins, consisting of a considerable *systolic jugular pulse* most pronounced in the deep veins in the neck In such cases the venous pulse pressure which is usually very small or nonexistent may be marked up to 50 or 60 mm and so striking that the jugular pulse may be wrongly interpreted as the carotid pulse (White and Cooke 1939)

Another interesting phenomenon consists of the *paradoxical inspiratory filling of the jugular veins* due to the inability of the right heart chambers either because of constrictive pericarditis or severe right heart failure or of an obstructed superior vena cava to pass on the extra blood they receive from the systemic veins as the result of the increased negative intrathoracic pressure during inspiration (Hitzig 1942)

In general the venous pressure determination is not of great clinical value inspection of the veins to determine their degree of engorgement usually sufficing without exact measurements It has been suggested however that a

figure of 20 cm of water of venous pressure in heart failure is a useful indication of the therapeutic need and value of venesection

We can now measure the blood pressure in the great veins in man by catheter and special manometer It varies normally in the human adult from +3 to +5 mm of mercury with great increase when the heart fails or in chronic constrictive pericarditis In the experimental animal the blood pressure in the great veins has been found to be much lower than that of the smaller veins dropping almost to zero in the venae cavae This is to be expected with the slowing of the blood stream resulting from the merging of many venous channels into the narrow limits of a few for even though these few are of large caliber their total capacity is far less than that of the peripheral veins Fortunately to aid in the return of blood to the heart there are four factors the most important of which is the intrathoracic negative pressure The effect of intrathoracic suction during inspiration is marked and in the experimental animal may more than quadruple the actual venous pressure in the great veins to establish the effective venous pressure For example in the dog a venous pressure of 10 mm (1 cm) of water may be increased through the action of this negative intrathoracic pressure to an effective pressure of 50 mm of water in the right atrium Poor action of the diaphragm and disturbances of respiration limiting the negative intrathoracic pressure and especially obstruction to the venous return flow to the heart through congestive heart failure chronic constrictive pericarditis pericardial effusions or mediastinal tumors or adhesions affect very easily and obviously the venous blood return to the heart on account of the low pressure that is usual in the great veins This is particularly true of the portal system where the blood has to flow through two sets of capillaries and enter the inferior vena cava by way of the hepatic veins which empty at a considerable angle into the vena cava

The three other factors aiding the return of venous blood to the heart are the tonus and movement of muscles which compress the veins the valves in the veins which help to keep the blood going in the right direction and on occasion as needed arteriolar and capillary dilatation to allow a speeding up of the blood flow into the veins and thence to the heart

For a discussion of capillary blood pressure see Chapter 8 under Capillary Circulation

BIBLIOGRAPHY

SPHYGMOMANOMETRY BLOOD PRESSURE, ARTERIAL (SYSTEMIC PULMONARY AND INTRACARDIAC) VENOUS AND LYMPHATIC

SEE ALSO GENERAL REFERENCES FOLLOWING CHAPTER 2 AND CHAPTER 19 SYSTEMIC HYPERTENSION

Arterial Pressure

Alvarez, W C. Blood Pressures in Fifteen Thousand University Freshmen." *Arch Int Med.*, 1923 XXXII 17
Alvarez, W C., and Stanley L. L. "Blood Pressure in Six Thousand Prisoners and Four Hundred Prison Guards A Statistical Analysis" *Arch Int Med* 1930 XLVI 17

Ayman D and Goldshine A D Blood Pressure Determinations by Patients w Essential Hypertension Difference Between Clinic and Home Readings Before Tre ment *Am J M Sc* 1940 CC 465

Ayman D and Krakower A "Influence of Sclerotic Arterial Wall on Blood Pressi Measurements Report of Case with Calcification of One Radial Artery *Arch I Med* 1933 LII 33

Bordley J III and Ragan C The Accuracy of Clinical Determinations of Arter Pressure *Tr A Am Physicians* 1941 LVI 222

Committees of the American Heart Association and Cardiac Society of Great Brit and Ireland Joint Report on the Standardization of Blood Pressure Reading *J A M A* 1939 CXIII 294 *Am Heart J* 1939 XVIII 95 *J A M A* 1951 CXLVII 6

Recommendations for Human Blood Pressure Determinations by Sphygmomano eters Committee under Chairmanship of Dr Carl J Wiggers Am Heart Assoc 19

Dameshek W and Loman J Direct Intra Arterial Blood Pressure Readings in Ma *Am J Physiol* 1932 CI 140

Erlanger J A New Instrument for Determining the Minimum and Maximum Blo Pressures in Man *Johns Hopkins Hosp Rep* 1904 XII 53

Gallavardin L and Tixier L La méthode auscultatoire moyen d étude du mode repletion artérielle trous auscultatoires *Paris med* 1920 X 25

Goldblatt H et al Studies on Experimental Hypertension I The Production Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemi *J Exper Med* 1934 LIX 347

Hales S *Statical Essays Containing Haemastaticks or an Account of Some Hydrau and Hydrostatical Experiments made on the Blood and Blood Vessels of Anima* W Innys and R Manby London 1733 Vol 2

Janeway T C Important Contributions to Clinical Medicine during the Past Thi Years from the Study of Human Blood Pressure *Bull Johns Hopkins Hosp* 19 XXVI 341

Korotkow Note on the demonstration of the auscultatory method of blood press determination in St Petersburg on October 20 1905 *Berichte d kaiserl Militarar Akad* St Petersburg 1905 XII 395

Marey E J Mesure manometrique de la pression du sang dans les arteres de l'homm *Physiologie experimentale* G Masson Paris 1876 p 309

Master A M Dublin L I and Marks H H 'The Normal Blood Pressure Rar and Its Clinical Implications *J A M A* 1950 CXLIII 1464

Pachon V Sur la methode des oscillations et les conditions correctes de son emploi sphygmomanométrie clinique *Compt rend Soc biol d Paris* 1909 LXVI 7

Oscillomètre sphygmometrique à grande sensibilite et à sensibilite constant *Ibid* p 776

Peterson L H Dripps R D and Risman G C A Method for Recording the A terial Pressure Pulse and Blood Pressure in Man *Am Heart J* 1949 XXXVII 7

Poiseuille J L M Recherches sur la force du coeur aortique *Magendie s jour de physiol* 1828 VIII 272 and 1829 IX 341

Riva Rocci S Un nuovo sfigmomanometro *Gaz med di Torino* 1896 XLVII 9

Segall H N Note on Measurement of Diastolic and Systolic Blood Pressure by Palp tion of the Arterial Vibrations (Sounds) over Brachial Artery *Canad M A* 1940 XLII 311

Smirk F H Casual and Basal Blood Pressures IV Their Relationship to the Sup plemental Pressure with a Note on Statistical Implications *Brit Heart J* 1944 VI 176

Steele J M "Comparison of Simultaneous Indirect (Auscultatory) and Direct (Intra arterial) Measurements of Arterial Pressure in Man *J Mt Sinai Hosp* 194? VIII 1042

Vaquez, H and Lajoie R J "The Physiological and Clinical Study of the Average Dynamic Blood Pressure (Pression Moyenne)" *Libman Anniversary Volumes* 19 III 1163

Vaquez H Gley P and Mouquin M Valeurs comparées de la mesure de la pression moyenne par les méthodes intra artérielle et oscillométrique" *Compt rend Soc de biol* 1933 CXIV 1305

Vierordt K *Die Lehre von Arterienpuls in gesunden und kranken Zustanden Gegrundet auf eine neue Methode der bildlichen Darstellung des menschlichen Pulses* F Vieweg u Sohn Braunschweig 1855

von Basch S Ueber die Messung des Blutdrucks am Menschen *Ztschr f klin Med* 1880 II 79

Einige Ergebnisse der Blutdruckmessung an Gesunden und Kranken *Ibid* 1881 III 50?

Der Sphygmomanometer und seine Verwerthung in der Praxis *Berlin klin Wchnschr* 1887 XXIV 179 206 224 244 and 285

Wendkos M H and Rossman P L The Normal Blood Pressure in the Lower Extremity *Am Heart J* 1943 XXVI 623

Wiggers C J Basic Hemodynamic Principles Essential to Interpretation of Cardio vascular Disorders *Bull New York Acad Med* 1942 XVIII 3

Wolf H J and Kindler K Zur Methodik der direkten Blutdruckmessung beim Menschen *Ztschr f d ges exper Med* 1934 XCIII 746

Venous Blood Pressure

Burch G E and Winsor T "The Phlebomanometer A New Apparatus for Direct Measurement of Venous Pressure in Large and Small Veins *J A M A* 1943 CXXIII 91

Eyster J A E *Clinical Aspects of Venous Pressure* Macmillan Co New York 1929

Frey A Ueber die Bedeutung der Venendruckmessung bei der diatetisch physikalischen Behandlung der Kreislaufstorungen *Deutsch Arch f klin Med* 1902 LXXIII 511

Gaertner G Ueber einen neuen Blutdruckmesser (Tonometer) *Wien klin Wchnschr* 1899 XII 696 and 717

Die Messung des Drucks im rechten Vorhof *Munch med Wchnschr* 1903 L 2038 2080 and 1904 LI 212

Griffith G C Chamberlain C T and Kitchell J R A Simplified Apparatus for Direct Venous Pressure Determination Modified from Moritz and v Tabora *Am J M Sc* 1934 CLXXXVII 371

Hitzig W M On Mechanisms of Inspiratory Filling of the Cervical Veins and Pulsus Paradoxus in Venous Hypertension *J Mt Sinai Hosp* 1942 VIII 625

Holt, J P The Measurement of Venous Pressure in Man Eliminating the Hydrostatic Factor *Am J Physiol* 1940 CXXX 635

Hooker D R and Eyster J A E An Instrument for the Determination of Venous Pressure in Man *Bull Johns Hopkins Hosp* 1908 XIX 274

Kendrew A The Graphic Registration of Venous Pressure in Man Illustrated by Some Observations on Reactive Hyperaemia *Heart* 1926 XIII 101

Moritz F and von Tabora D Uber eine Methode beim Menschen den Druck in oberflachlichen Venen exakt zu bestimmen *Deutsch Arch f klin Med* 1910 XCVIII 475

White P D and Cooke W T The Recognition and Significance of Marked and Chronic Systolic Pulsation of the Deep Jugular Veins *Tr A Am Physicians* 1939 LIV 199

Winsor T and Burch G E Use of the Phlebomanometer Normal Venous Pressure Values and a Study of Certain Clinical Aspects of Venous Hypertension in Man. *Am Heart J* 1946 XXXI 387

von Recklinghausen H Ueber Blutdruckmessung beim Menschen *Arch f exper Path u Pharmakol* 1901 XLVI 78

Unblutige Blutdruckmessung *Arch f exper Path u Pharmakol* 1906 LV 375 and 412 *Neue Wege der Blutdruckmessung* Julius Springer Berlin 1931

Capillary Pressure (See also references under Capillary Circulation in Bibliography of Chapter 8)

Eichna L W and Bordley J III Capillary Blood Pressure in Man Comparison of Direct and Indirect Methods of Measurement *J Clin Investigation* 1939 XVIII 695

Landis E M Micro Injection Studies of Capillary Blood Pressure in Human Skin *Heart* 1930 XV 209

Lombard W P The Blood Pressure in the Arterioles Capillaries and Sm of the Human Skin *Am J Physiol* 1911-12 XXIX 335

Intracardiac Pressure and Pulmonary Blood Pressure

Cournand A Lauson H D Bloomfield R A Breed E S and Baldwin "Recording of Right Heart Pressures in Man *Proc Soc Exper Biol & Me* LV 34

Dexter L Haynes F W Burwell C S Eppinger E C Sagerson R P an J M Studies of Congenital Heart Disease II Pressure and Oxygen Conte Blood in the Right Auricle Right Ventricle Pulmonary Artery in Control with Observations on the Oxygen Saturation and Source of Pulmonary Blood *J Clin Investigation* 1947 XXVI 554

Hamilton W F Brewer G and Brotman I Pressure Pulse Contours in t Animal I Analytical Description of a High Frequency Hypodermic Manom Illustrative Curves of Simultaneous Arterial and Intracardiac Pressures" *Physiol* 1934 CVII 427

Lenegre J and Maurice P Premieres recherches sur la pression ventriculair *Arch d mal d coeur* 1944 XXXVII 101

La pression ventriculaire droite *Paris med* 1945 CXXIX 21

"Recherches sur la pression sanguine dans la petite circulation chez l *Acta Cardiologica* 1947 II 1

Richards D W Jr et al Pressure of Blood in Right Auricle in Animals Man Under Normal Conditions and in Right Heart Failure *Am J Physi* CXXXVI 115

Lymphatic Pressure

Drinker C K Warren M F Maurer F W and McCarrell J D 'The Fl sure and Composition of Cardiac Lymph *Am J Physiol* 1940 CXX 4

CHAPTER 7

CARDIOVASCULAR ROENTGENOLOGY

In the present edition this chapter has been profitably shortened several helpful new illustrations have been added and a number of pertinent references to the literature published since 1943 have been appended to the Bibliography

Williams F H Notes on X Rays in Medicine *Tr A Am Physicians* 1896 XI 375

During the past two or three months I have been much interested in studying the X rays and with the assistance of Mr C L Norton and Mr R R Lawrence of the Massachusetts Institute of Technonogy who have been investigating the X ray problem in the Rogers Laboratory of Physics have tested the application of X rays to medicine in various ways Their application to surgery was soon evident

But I wish especially to direct your attention to some of the medical rather than the surgical uses of these magical rays and especially to their use with the fluoroscope in the fluoroscope with a screen of tungstate of calcium the parts of the body which are most easily passed by the X rays appear lightest on the screen those which are densest being darker The lungs are easily penetrated

The pulsations of the heart may be followed with the fluoroscope not only the ventricular but also the auricular contractions and dilatations

In the following cases the usual physical examination and that made with the fluoroscope corresponded very well

Case I —The first medical case I examined was that of a man with an enlarged heart (seven inches in transverse diameter) I found that the outline of the heart as seen from the front of the body through the fluoroscope corresponded in a general way to the outline drawn on the skin with percussion as a guide It was interesting to note that the heart could be made out through the man s waistcoat and two shirts

INTRODUCTION

Cardiovascular roentgenology (*Rontgen* 1895 and λογος knowledge) or radiology (*radius* ray and λογο knowledge) has become firmly entrenched as an important part of routine study of the heart and blood vessels it ranks

fourth in value as a method of examination after history taking physical ex amination and electrocardiography Although in cardiovascular diagnosis th roentgen ray usually supplies but confirmatory evidence sometimes surprisin and frequently useful and interesting information results from such routin study Only by this method may the size and shape of the heart be determine with certainty during life the size and shape of the left atrium aorta an lung hiluses be ascertained at all and calcification in pericardium hear muscle valves or deep blood vessels be actually visualized On the other hand

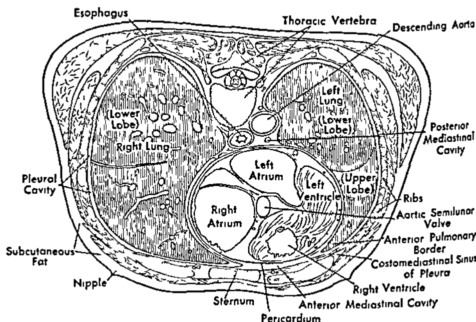


FIG 20 Anatomic drawing showing cross (horizontal) section of thorax and heart at level of the eighth thoracic vertebra (Sobotta and McMurrich *Atlas and Textbook of Human Anatomy* 1906 Kindness of W B Saunders Company Philadelphia)

it must be admitted that serious heart disease may be present as discovered in other ways when no clue is given to its presence by roentgenology Also early and slight cardiovascular lesions usually escape notice in the roentgen ray film because the heart and vessels may show no definite abnormalities of size shape, or action For the most part therefore roentgenology merely reveals evidence of well established or advanced disease which is difficult or im possible to eradicate Yet it does help the practitioner of medicine appreciably in the establishment of exact diagnosis which are so essential to accuracy of prognosis and to the handling of patients with chronic heart disease

The chief difficulty in the routine application of roentgenology to the circu lation lies not in the technic which can be mastered without great difficulty but in the interpretation of the normal limits of heart size shape and action and therefore in the diagnosis of slight abnormalities There are so many factors for example age size build respiration and nervousness resulting in in

dividual variations within the normal (see Figures 2 3 and 6 in Chapter 2) that it is at present impossible to recognize them all or at least to take them all into consideration in the establishment of any satisfactory tables of measurement of size or rules about shape or action Not only are the normal limits difficult or impossible to define accurately but in a given individual important changes may occur in heart size or shape insufficient to produce definite roentgenologic abnormalities at the time of examination which would be noted if comparative studies had been previously made For example a heart showing in an anteroposterior teleroentgenogram a shadow area of 80 sq cm at the lower limit of the normal figures may increase in area 38 per cent before it equals even the average normal measurement (110 sq cm) and as much as 75 per cent before it equals the upper normal limit of 140 sq cm in the case of a person with a body surface area of 1 8 sq meters (Smith and Bloedorn 1922) Successive records of heart size and shape in the same individual carefully made under varying conditions of health should be more useful than a single comparison of this individual case with a table of normal averages or a set of rules it is however often impossible to possess information about the roentgen ray findings prior to the onset of trouble in a given case In spite of these difficulties some rules are necessary and normal standards for measurements of size are useful if we realize their inaccuracy in application to individual patients and do not lull ourselves into a false sense of security which tends to develop from the use of figures and formulas

METHODS OF CARDIOVASCULAR ROENTGENOLOGY

Roentgenology of the heart includes seven procedures the first three of which are commonly used and the last four in special cases or for some particular study They are as follows (1) fluoroscopic examination (2) orthodiagraphy (3) teleroentgenography (teleradiography) (4) (roentgen) kymography (5) (roentgen) tomography (planigraphy) (6) visualization of heart chambers and greater and lesser arteries and veins by the injection of radio-opaque media (e g Diodrast) into the blood stream and (7) roentgencinematography At the present time the first method is used universally by the most careful workers everywhere but the other methods are rarely used together There is a division into two schools that employing orthodiagraphy and that using teleroentgenography Each of these methods has certain advantages which will be presented below but in each case fluoroscopy should be and ordinarily is employed along with either orthodiagraphy or teleroentgenography The seven procedures mentioned above will be briefly summarized herewith

1 **Fluoroscopy** (φλυειν to flow out ροη current and σκοπειν to examine) Fluoroscopic examination consists in the study on the fluorescent screen of the projection of the heart shadow in its various parts and in toto and with the thorax of the subject in various positions in contact with the screen If possible the subject should in harmony with several other methods of ex

amination—inspection percussion and auscultation—be examined chiefly in the upright position Although the tube may be placed at a distance (2 meters or more) from the thorax for the purpose of seeing the heart and great vessel relatively undistorted by divergence of rays (telefluoroscopy), as in the case of teleroentgenography this is not essential inasmuch as accurate measurements can be obtained by orthodiagraphy nor is it practicable since so much extra energy is required (about 16 times as much as is needed with the tube at 50 cm) In fact the very magnification of the details and activity of the heart shadow by the divergent rays is helpful and one quickly becomes accustomed to the degree of distortion Also the illumination is better with the tube nearer than at a distance especially in the oblique or lateral views

The first position studied is most conveniently the *anteroposterior*[1] with the patient erect facing the observer squarely and leaning his anterior chest wall against the screen with the tube behind him After all parts of the heart and great vessel shadows have been carefully examined in this position the contour and action of the whole heart observed the action of the diaphragm noted along with the effect of deep inspiration and expiration and the lung shadows and especially the hiluses studied the patient should then be rotated slightly to the left so that the right anterior side of the chest wall touches the screen This is called the *right anterior* or *first oblique position* To improve the view in this position the right hand should be held behind the head and the left hand on the left hip with the elbow forward Still further rotation in the same direction to the *right lateral* and *right posterior oblique positions* may then be carried out if desired but this is usually not necessary study in the right anterior oblique position sufficing In a similar way the patient is rotated to the right from the anteroposterior position until the left anterior part of the chest wall touches the screen This is called the *left anterior* or *second oblique position* The left hand should be held behind the head and the right hand on the right hip Again further rotation in the same direction may be carried out if desired to the *left lateral* and *left posterior oblique positions* And finally the patient may be examined with his back squarely against the fluoroscopic screen in the *posteroanterior position* to emphazie abnormalities of the descending thoracic aorta but this position is rarely of any value For routine fluoroscopic examination the three positions anteroposterior right anterior oblique and left anterior oblique ordinarily suffice An important part of the whole examination includes careful observation of heart and vessel shadows during the process of rotation from one position to another this may explain certain abnormalities the cause of which is not obvious in the positions themselves Fluoroscopic tracings not orthodiagraphic are sometimes

[1] Throughout the book the position of the subject in roentgenologic examination is designated according to the axis termination at the screen or film as has been customary and not at the tube thus anteroposterior signifies that the front of the chest rests against the screen "right anterior oblique means that the right anterior chest wall is against the screen and so on If the designation "posteroanterior is employed in the place of the customary "anteroposterior" "left posterior oblique must be similarly employed instead of right anterior oblique to be consistent but this change is neither necessary nor convenient

made in one or more positions to study outline shapes but these are of limited value

2 **Orthodiagraphy** (ορθος straight δια through and γραφειν to write) (Moritz 1902) An orthodiagram is a tracing made by the observer of the shadow of the heart and great vessels outlined against the fluoroscopic screen by the *central rays* from the roentgen tube Its advantages are that it is very accurate if well done because the rays used are exactly parallel that observation of the heart in action allows accurate determination of the position of the apex and of junctions of atria and ventricles or of great vessels and heart which may not be possible in any other way that it requires fluoroscopic observation not always carried out with teleroentgenography and finally that it is an inexpensive method of obtaining permanent records of the shadow of the heart and great vessels It has the disadvantages of incompleteness of total detailed picture of heart and thorax and of easy possibility of subjective errors in untrained or careless hands

3 **Teleroentgenography** (τηλε far away *Rontgen* the discoverer and γραφειν to write) or teleradiography (Kohler 1905) The other method in routine use for obtaining a graphic record of the heart shadow by roentgen ray from which a fairly accurate idea of heart size and shape can be obtained is teleroentgenography (teleradiography) A teleroentgenogram is a record on film or plate of the shadow in whole or in part of the heart and great vessels cast by the roentgen rays with the tube far enough away (2 meters or 6 to 7 ft) from the chest and plate for reasonable accuracy At 6 to 7 ft the error of heart size measurement is however still appreciable the excess in transverse cardiac diameter in the normal adult being from 1 0 to 1 5 cm (8 to 12 per cent) and as great sometimes in pathologic cases as 2 5 cm the excess is still more evident in the measurement of surface area Certain factors enter in as variables to increase or to decrease this error They are chiefly heart size and thickness of the anterior chest wall The larger the heart the greater is the error because the rays outlining its shadow are more divergent than are those outlining the shadow of a small heart Even the ratio of heart size to thorax size (the cardiothoracic ratio) differs in the two technics being slightly less in teleroentgenography than in orthodiagraphy because the maximal frontal plane of the heart lies anteriorly to that of the thorax (see Figure 20 page 126) The advantages of the teleroentgenogram are as follows (1) it is a more objective record than an orthodiagram and so less liable to subjective sources of error provided the technic be accurate (2) it is a more complete record than the orthodiagram giving greater detail and demonstrating clearly differences in position of the thorax which differences may render inaccurate comparative measurements of heart size at different times (3) it outlines more clearly hazy or otherwise indefinite borders (4) it can be satisfactorily carried out by a well trained and careful technician the actual measurements and interpretation being made from the finished film by the physician

4 **Kymography** (κυμα wave and γραφειν to write) About twenty years ago there was introduced (Stumpf 1931) an ingenious application of roent

genography to the study of the degree and direction of pulsation of the hear and great vessels first suggested by Sabat (1913) By the use of a grid o lead strips with narrow slits between them it is possible to record the systoli and diastolic heart and vessel borders of limited alternating sections of th heart shadow when the film moves at a uniform rate across the slits at a speed which allows several pulsations to be recorded for each of the shadow sections The grid may be placed vertically, diagonally or radially and the screen o the grid may move in any direction but the usual and most practicable an instructive arrangement is for the grid to be fixed in place with the slit horizontal and for the film to descend vertically In the resulting kymogram (see Figure 21) the innermost limits (valleys) of the excursions normally represent systole in the case of the heart shadow and diastole in that of the shadows of the great vessels while the outermost limits (peaks) normally represent diastole in the case of the heart shadow and systole in that of the shadows of the great vessels In certain disease conditions there are distortions of these pulsations an increase, for example in cases of aortic regurgitation so far as left ventricle and aorta are concerned, or of the whole heart and both aorta and pulmonary artery in thyrotoxicosis a decrease in cases of great myocardial weakness myxedema or constricting pericardium or an absence or even a reversal of the pulsation (called paradoxical) of a limited portion of the left heart shadow border at or more often just above the apex in the case of a moderately large cardiac aneurysm or myocardial infarct There is not a great deal of clinical value in roentgenkymography except in occasional confirmation or discovery of a myocardial infarct from coronary occlusion the differentiation at times of aortic aneurysms from other types of mediastinal tumors the separation of the shadows of atria and ventricles and in the course of complete study of rare or puzzling cases

An interesting new method of recording the action of the heart fluoroscopically has been introduced through Chamberlain by Henny and Boone (1945) by the use of the photoelectric cell placed over any desired portion of the heart border and connected with galvanometer Simultaneous tracings can be made of the electrocardiogram or of carotid pulse or heartbeat itself also recorded electrically Figure 22 shows examples of normal and abnormal curves which have been variously called *electrokymograms* or *electrofluorograms* Not only may records be made of the pulsation of atrial and ventricular borders and of that of the great vessels superior vena cava aorta pulmonary artery and its branches in the lung hiluses but so-called *densograms* can also be made over the main heart shadow itself and over the lungs presenting curves of the variations in the thickness of the underlying mass These electrokymograms present a clearer and simpler record of the cardiovascular motions than the films that have been customarily taken in the past (Figure 21) and will probably supersede them They have the same function however in revealing or confirming such diagnoses as myocardial infarction of significant extent and of certain aneurysmal dilatations of the great vessels Also they have been used in an effort to measure the stroke volume of the heart

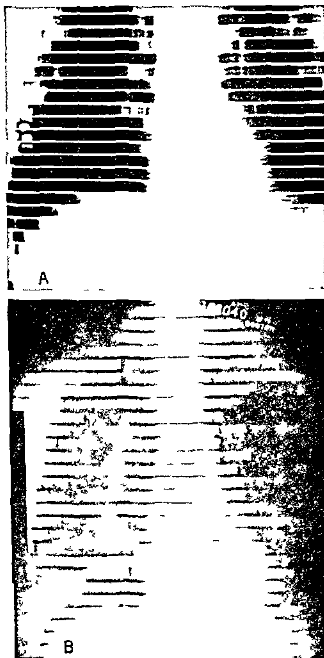


FIG 71 Kymograms (roentgenograms) of thoraces of (*A*) normal individual (kindness of Dr Richard Schatzki Mt Auburn Hospital Cambridge Mass) (*B*) case with myocardial infarct (kindness of Dr George Levene Massachusetts Memorial Hospital Boston)

5 **Roentgentomography** (*Roentgen* τομος a cut or section and γραφειν to write) or laminagraphy (Latin *lamina* layer and γραφειν), or planigraphy (Latin *planus* a level and γραφειν) There has also been introduced in recent years a method of x ray study of the thorax that is helpful particularly in locating in three dimensions the exact position of lesions in the lungs It is of much less importance so far as the heart is concerned but the method has not in that direction been wholly explored as yet Tomography consists in the

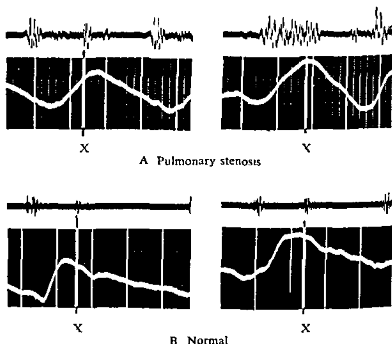


FIG 22 Electrokymograms and simultaneous phonocardiograms taken at the pulmonary valve area of (A) two patients with pulmonary stenosis and (B) two normal individuals Note the slow upstroke in the electrokymogram of the two patients with pulmonary stenosis Time = 0 04 and 0 20 second X = time of second heart sound (Kindness of Mr M A Rappaport Sanborn Company Cambridge)

recording of body shadows at varying depths by exact focusing of the x ray —thus the anterior and posterior regions of the thorax may be blurred while a sharp outline is obtained of a vertical frontal plane in midthorax It is possible by this means to obtain clearer pictures of the atria and pulmonary vessel or of the aortic arch or descending aorta

6 **Radio opaque visualization** In obscure or special cases the injection of a radio-opaque medium most commonly Diodrast into veins or arteries of arms or legs and very recently even directly into the ventricles themselves (Ponsdomenech and Nuñez 1951) has proved helpful in establishing a detailed diagnosis of abnormalities of blood vessels or heart chambers that might be impossible in any other way (Figures 23 24 and 148 page 779) Considerable experience in both injection and roentgenographic technic is neces



FIG 73 Roentgen films of chest of male age 40 with shadow in region of aortic arch (*A*) Anteroposterior view (*B*) Left anterior oblique view immediately after Diodrast injection showing filling of right ventricle and pulmonary arterial tree (*C*) Film a few seconds later showing filling of the left ventricle and aorta This method of technic of Diodrast injection establishes at once the diagnosis of mediastinal tumor versus aortic aneurysm (Kindness of Dr B J Walsh Washington D C)




A




B

FIG 24 (*A*) Diodrast x ray pictures showing the filled right ventricle and pulmonary artery in the anteroposterior and left anterior oblique views in the case of a normal heart (*B*) Diodrast x ray pictures showing the filled left ventricle in the case of a normal heart with diseased right lung (Kindness of Dr E R Ponsdomenech and Dr V B Nunez Havana Cuba)

sary to obtain the best results but the method should be made available in every teaching hospital and is helpful in differential diagnosis especially in congenital heart disease

7 **Roentgencinematography** Finally a seventh method of roentgen ray study of the heart of interest from the standpoint of special investigation or teaching is that of cinematography The most practicable way which has recently been developed consists of cinematography of the shadow as it is seen on the fluoroscopic screen (Reynolds R J 1934 Janker R, 1936 Rushmer 1949)

THE SHAPE SIZE AND ACTIVITY OF NORMAL HEART AND GREAT VESSELS STUDIED BY ROENTGEN RAY

The shape of the normal roentgen ray heart shadow is quite variable being dependent on a number of factors The heart shadow should be outlined during quiet respiration and preferably in the sitting position for forced respiration causes abnormalities of shape and size and the standing and recumbent positions may appreciably affect the heart Marked changes have been experimentally produced by certain respiratory efforts the heart shadow increasing considerably in size with the Muller experiment (an attempt to inspire forcefully with the glottis closed) and decreasing considerably in size sometimes to appear like the cor pendulosum (pendulum heart) with the Valsalva experiment (an attempt to expire forcefully with the glottis closed) a fact of considerable interest (Crowden and Harris 1929) such experiments produce however very artificial conditions not comparable to clinical findings The decrease in heart size during the Valsalva experiment is due to the prevention of entrance of blood into the heart by the increased intrathoracic pressure while the increase in heart size during the Muller experiment is due to the increased flow of blood into the heart resulting from the markedly negative intrathoracic pressure So far as position of the subject is concerned the heart size and therefore its shadow may be considerably decreased in the standing position (due to much decrease in the return of blood to the heart in that posture) while there may be a considerably increased return of blood to the heart and increased content of blood in the lung vessels in the recumbent position resulting in a physiologic dilatation (Zdansky 1936) In reporting or recording roentgen views of the heart a statement should always be made as to the position of the patient and also the phase or state of respiration To study the heart (in contrast to the lungs) it is best to make the examination and the films during very quiet respiration which is essentially midway between full inspiration and full expiration There can be great distortion of the heart shadow with marked decrease in size if the films are taken while the breath is held in full inspiration a common practice in study of the lungs (Figure 3C page 32) For further observations concerning the range of the normal heart the reader is referred to Chapter 2

Anteroposterior view In the anteroposterior view the shadow of heart and

great vessels is roughly egg shaped with apex diagonally down and to th subject s left and with the great vessels attached as a pedicle at the left sid of the base (Figure 25) If the diaphragm is high the heart lies more hori zontally and to the left and there is a more acute angle between it and th great vessels (Figure 3 page 32), if the diaphragm is low the heart lie more vertically and centrally in the body seems narrower (because of thi change of position and of the resultant rotation to the left) and hangs dow from the great vessels with much flattened angle (Figure 3)

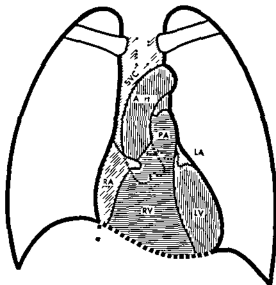


FIG 25 Drawing of normal x ray heart shadow with the various chambers and grea vessels indicated (Kindness of Sir John Parkinson and the *Lancet* London)

SVC	*superior vena cava*	*RV*	*right ventricle*
PA	pulmonary artery	LA	left atrium
RA	right atrium	LV	left ventricle

The borders of the anteroposterior shadow of the heart and great vessel are three in number because of the roughly triangular shape they are right left and inferior Unless concealed by abnormal shadows in lungs pleurae pericardium or mediastinum the right and left borders are easily seen The inferior border is seen with difficulty or not at all concealed as it is by intra abdominal shadows unless there is sufficient air in stomach or intestines to make its outline visible Its whole extent is seen in only two conditions (1) pneumoperitoneum and (2) interpolation of colon between heart and liver The upper border of the heart at the junction of the great vessels is not seen except at its outer ends

1 *The right border* (that to the right of the sternum of the subject *not* on the observer s right) is composed of three parts The uppermost is a rather faint straight vertical edge extending slightly outward and to the right from below up and not always clear It is produced by the shadow of the

right border of the superior vena cava and innominate vein at the upper part overlying the innominate artery the artery itself if dilated or prominent may form the shadow edge The second part (next in order below) is the straight edge of the superior vena cava or more commonly the slightly convex shadow of the right edge of the ascending aorta superimposed on the superior vena cava shadow and making up a second quarter or more of the whole right border the inwardly directed curve of this aortic shadow to the left can often be made out overlying the fainter shadow of the vena cava The third part of the right border of the heart shadow is the moderately convex shadow of the right edge of the right atrium from a point just below the mouth of the superior vena cava down to the inferior vena cava which can in rare instances be barely seen as a very short straight line quickly disappearing into the shadow of the diaphragm this right atrial shadow makes up the lower third to half of the right border of the shadow of the heart and great vessels

2 *The left border* of the shadow of the heart and great vessels is considerably longer than the right (about 50 per cent longer) and is made up normally of four parts The uppermost part is a short convex curve close to the apex of the whole shadow and is directed up toward the left shoulder of the subject it is variable in prominence and is due to the shadow of the upper and left edges of the aortic arch and beginning of the descending aorta The second part is a slightly convex curve just below usually slightly longer than the first but making a considerable angle with it directed downward from the subject s right to his left and often almost continuous in direction with the left border of the main shadow of the heart itself which lies below the trunk of the pulmonary artery and its left main branch cause this convexity Third and next below for a very short distance and forming a straight or slightly convex line lies the left border of the left atrial appendage often not distinguishable from the edge below it unless its presystolic pulsation happens to be seen or there is marked left atrial bulging And fourth the major part, two thirds to three fifths of the left heart and great vessel shadow border is caused normally by the left ventricular shadow forming a slightly or moderately convex line sloping to the subject s left from above downward and becoming more definitely curved downward as the apex is approached

3 When *the lower border* of the heart shadow is visible it is made up of the apex and lower border of the left ventricle on the extreme left then for one half to three quarters of the distance to the subject s right heart border it is caused by the right ventricular shadow and for the rest of the distance to the right of the midsternum by the right atrium However varying positions of the heart alter these relations for example in the case of the drop or vertical heart little or none of the right atrium forms the lower border of the heart shadow When this lower border is visible it is slightly convex near the apex but fairly straight from there on

The peak of the heart and great vessel shadow is blunt and obscure except where the aortic arch is visible on the subject s left, but in some cases the aorta crossing above the pulmonary artery to form the arch can be seen This

peak of the great vessel shadow is more cylindric than cone shaped being an elongated pedicle

Right anterior oblique view In the right anterior or first oblique view (Figure 26) the shadow of the heart and great vessels shows in front from below upward the convex curve of the right ventricle if the subject is sufficiently turned if the rotation is slight the left ventricle may be seen At the upper third of this anterior edge the pulmonary artery and aortic shadows appear and the latter sweeping over in a long curve loses itself in the shadow

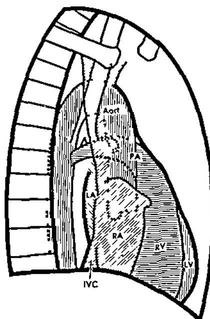


FIG 26 Drawing of shadows of normal heart and great vessels in right anterior oblique position with various chambers and great vessels indicated (Kindness of Sir John Parkinson and the *Lancet* London)

IVC inferior vena cava	RA right atrium
PA pulmonary artery	RV right ventricle
LA left atrium	LV left ventricle

of the spine posteriorly Under this aortic shadow and at the upper part of the posterior border of the heart shadow lie the bifurcations of the trachea and of the pulmonary artery Below this are the straight or slightly convex borders of the two atria the left above the right and the latter extending down to the diaphragmatic shadow where the inferior vena cava may be just visible The anterior and posterior mediastinal spaces should be clear and the trachea and bronchi are usually to be seen The left ventricle is concealed at the back of the heart shadow in this position (note Figure 20)

Left anterior oblique view In the left anterior oblique view (Figure 27) the heart is seen as it were almost in sagittal section both ventricles and both atria being evident the two former making up the lower two thirds of the

heart shadow the right in front and the left in back and the two latter making up the upper third of the shadow, the right in front and the left behind The aorta arches over the top its whole extent may be seen better in this view than in any other if it is sclerotic but normally the outline of the lower border of the aortic arch is made out with great difficulty if at all Below the aorta at the upper limit of the heart shadow posteriorly is the pulmonary artery Between the aortic arch and the pulmonary arch is a clear space called the aortic window

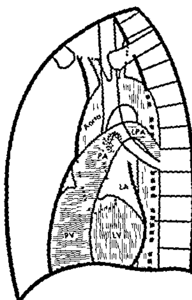


FIG 27 Drawing of shadows of normal heart and great vessels in left anterior oblique position with various chambers and great vessels indicated (Kindness of Sir John Parkinson and the *Lancet* London)

PA pulmonary artery
LPA left pulmonary artery
LA Left atrium
RV right ventricle
LV left ventricle

Note aortic window (open space) separating aortic arch from pulmonary arteries

The chief advantage of the oblique views lies in the study of aorta and left atrium this is especially true of the left anterior oblique view which has been regarded by some workers as the most valuable of all views in establishing the comparative size of the various parts of the heart

Lateral view The lateral view is of value in measuring the depth that is the anteroposterior diameter of the heart for its own value or for use in a formula to estimate the heart volume (see page 146) This diameter is taken at right angles to the long axis of the heart

Normal size of heart and great vessels Certain measurements of heart size made on the orthodiagram or teleroentgenogram are in routine use and are of some value in spite of the wide normal variations and of the difficulty or

impossibility of judging accurately either the presence or degree of slight cardiac enlargement by such measurements It is obvious for example th: increase in heart volume is represented by a far smaller increase in measure ments of diameters or of area an increase of 100 cc of volume would ad only about 15 sq cm to the area in the anteroposterior view

The following are the more useful teleroentgenographic measurements a but two obtained in the anteroposterior view to make correction for orth diagraphic records subtract 10 per cent Other measurements of all sorts ha been suggested but only the more important or interesting will be mention here

The *transverse diameter* of the heart (T or H—Horizontal—of Bordet) made up of the sum of the maximal distance of the right border from t midsternum (MR) and of the maximal distance of the left border from t midsternum (ML) Normally this diameter measures in the adult from to 15 cm depending on the size of the person and from 6 to 10 cm in t child

The *long diameter* of the heart (L) is the distance from the junction right atrial and great vessel shadows on the right border to the point of t cardiac apex Normally this diameter measures in the adult 1 0 to 1 5 more than the transverse diameter on the average therefore from 11 to cm and in the child 0 5 to 1 0 cm more than the transverse diameter that from 7 to 11 cm

The *broad diameter* of the heart (B) is made up of the addition of t lengths of two perpendiculars dropped from the line of the long diameter the junction of right atrial shadow and diaphragm on the right (BR) and the junction of left atrial (or left ventricular) and pulmonary artery (or rig ventricular) shadows on the left (BL) Normally this diameter measures the adult 8 to 11 cm and in the child 5 to 8 cm

The *left ventricular chord* (LV or VG—*ventricule gauche*—of Bord subtends the arc of the left ventricle from its upper extremity on the left the apex Normally this chord measures in the adult from 5 to 9 cm and in the child from 3 to 5 cm

Width of the great vessels (GV) A measurement of some interest but not of much value is that of the width of the shadow made by the great vessels at the widest part of the pedicle of the heart shadow usually at the level of the second intercostal space horizontally measured This measurement varies not only with dilatation of the aorta and superior vena cava but also with kinking of the aorta when it is very tortuous from arteriosclerosis or pushed upward by an enlarged or horizontally placed heart resting on a high dia phragm Normally the width of the great vessels measures 5 to 7 cm in the adult and 3 to 4 cm in the child of ten years of age

The *diameter of the aortic arch* (Ao) taken in the anteroposterior posi tion is a measure of the length of the horizontal line drawn from the outer most bulge of the aortic shadow at the left of the midsternum to the shadow of the barium filled esophagus which passing under the aortic arch outlines

he right border of the descending portion of the arch a subtraction of 2 mm s necessary to take into account the *thickness of the wall of the esophagus* If this line is not horizontal the measurement is inaccurate because of abnormal relative positions of aorta and esophagus The normal *upper limit* of this aortic arch measurement in the adult should not be over 3 cm The diameter of the aorta at the beginning of the arch (Ao or Asc A) is found in the right anterior oblique position by measurement of the horizontal line joining the two sides the anterior edge outlined by the anterior mediastinum and the posterior edge by the trachea Two millimeters comprising the thickness of the tracheal wall should be subtracted from this measurement to obtain the true *aortic diameter* which should normally range from 2 5 to 3 5 cm at this point An unsatisfactory measurement of the diameter of the aortic arch is that obtained *in the left anterior oblique position* namely the vertical distance from top to bottom of the aortic arch shadow at the top of its curve This in the normal adult averages 3 0 to 3 5 cm *It is unsatisfactory* because often the lower border of the aortic arch is seen only with great difficulty if at all unless a contrast medium has been injected

The *depth of the heart* (or anteroposterior diameter) is measured at right angles to the long axis of the heart in the lateral view at the point of greatest *thickness* Normally this measures two thirds to three quarters of the transverse diameter of the heart in the anteroposterior view (Roesler 1934) or in the adult 6 5 to 10 5 cm and in the child 4 to 7 cm Its chief value is in checking the significance of the measurement of the diameters of the anteroposterior view and in forming *a part of a formula for estimating the volume of the heart*

A standard but often unsatisfactory measurement of chest size for comparison with heart size is the *internal diameter of the thorax* (Th) *at its widest* point just above the diaphragmatic attachment

The *area* of the heart shadow (A) which does not include the great vessels is measured after arbitrarily joining by slightly convex lines the outer and visible ends of the upper and lower borders The area can be easily determined by the use of a planimeter less easily by superimposition of cardiac outline on paper specially ruled with centimeter squares or by weight of paper cut out exactly to fit heart *shadow compared to weight* of 100 sq cm of the same paper (Mazer 1942) but most easily by nomogram based on the broad and long diameters of the heart (Ungerleider and Gubner 1942) *The area of the normal* heart shadow in the anteroposterior teleroentgenogram measures in the adult from 65 to 145 sq cm averaging 112 for males and 100 for females and in the newborn from 17 to 20 sq cm

Finally attempts have been made to obtain a measurement of *heart volume* by the use of various formulas Such measurement theoretically ideal has not as yet proved practical it will be discussed below The range of the normal heart volume in the adult male is from 400 to 900 cc and in the adult female from 300 to 550 cc (Comeau and White 1939)

When the heart lies horizontally the transverse and long diameters become more nearly the same A correction of the normal transverse measurement for

position has been suggested based on the angle between the lines of these diameters and utilizing the surface area of the body for standard compari The smaller the angle and also of course the larger the surface area of body the longer should be the transverse diameter Figure 28A shows average normal measurements of the transverse diameter with these two ables charted and Figure 28B shows the surface area of the subject in sq meters calculated according to height and weight This latter figure may be used in calculating the normal vital capacity (see Chapter 10)

The relationship of depth or thickness of the heart to the size of the and diameters on the frontal plane silhouette is of much interest and of fu mental importance The flatter the chest the less is the depth of the heart the greater are the various frontal plane measurements the deeper the c the smaller should be the frontal plane measurements of the heart (Roe 1934)

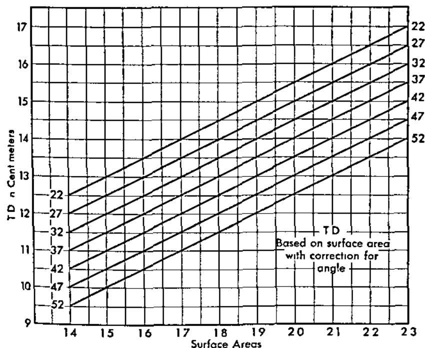
Calculation of normal heart measurements The simplest most pract and most reliable heart measurements are those of the *diameters* transv long broad and anteroposterior (or depth) They are measured directly usually with ease The transverse diameter is the most useful of the diame the anteroposterior the least used Tables slide rules and nomograms (Ho and Eyster 1926 Ungerleider and Gubner 1942 Kurtz 1943) have constructed for the calculation of the normal average transverse dian according to height and weight for comparison with the actual finding in given case (Figure 29) The range of normal varies from 10 per cent a to 10 per cent below this figure a fact that materially diminishes the valu this as well as all other roentgen measurements as utilized at present Chapter 2)

A roentgen measurement of heart size very popular in the past but gene unreliable and unsatisfactory because of the extremely wide range of normal (from 33 to 57 per cent) is the so-called *cardiothoracic rati heart lung quotient* using a fraction in which the numerator is the transv diameter of the heart and the denominator the internal diameter of the thc the normal range is from 0 33 to 0 55 Not only is the range of normal wide because of the poor correlative standard of thoracic width (height weight are preferable although also open to objection) but the cardiothoi ratio has in addition the defect inherent in the transverse diameter which not take into consideration the broad diameter of the heart which ma considerably increased in mitral stenosis for example without increas the transverse diameter There are however rare persons of unusual b short and light with wide chests in whom the cardiothoracic ratio applies r accurately than do other formulas

The other diameters especially the long and the broad are usefu supplements of the transverse but are more readily considered in connec... with area measurements either made directly or by formula as in the nomogram in Figure 29

The measurement of the *area* of the heart shadow in the frontal silhouette

A



B

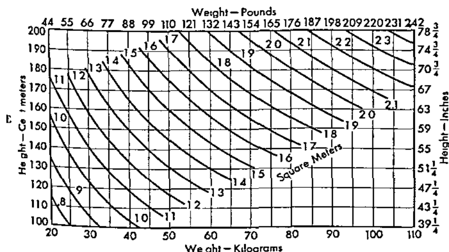


FIG ?8 Corrections for angle of heart s axis (*A*) Chart for the determination of the normal variation of the measurement of the transverse diameter (T D) of the roentgen heart shadow with varying height and weight (Smith and Bloedorn *U.S Naval M Bull* 19? XVI ?19)

(*B*) Chart for the determination of the surface area of the body from the height and weight (Dubois E F Fig 19 on page 119 of *Basal Metabolism in Health and Disease* ?nd ed Lea & Febiger Philadelphia 1927

that is on the usual anteroposterior teleroentgenogram or orthodiagram is theoretically sounder than that of the diameters and actually it has been found to be fairly satisfactory when compared to the size of the individual as in the formula *orthodiagraphic cardiac area in sq cm = age × 0 0704 + stature × 0 8668 + weight × 0 337 minus the constant 63 8049* (Hodges and

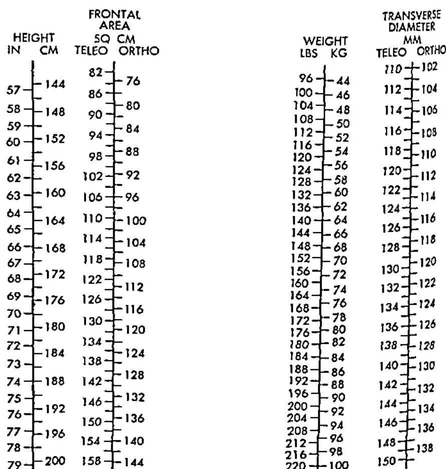


FIG 29A Nomograms for determination of the frontal area and transverse diamete of the normal heart shadow of teleroentgenogram and orthodiagram predicted fron height and weight

The Hodges Eyster formula applied by Kurtz The roentgen films and orthodiagram were made during quiet respiration Add 10 per cent of patient s age to predicted trans verse diameter The measurement of the area by teleroentgenogram is 11 per cen greater than the area of the heart shadow by orthodiagram The transverse diamete of the heart shadow in the teleroentgenogram is 8 per cent greater than that of th orthodiagram

In making the determination a straight edge joins the figures for the height and weigh of a given case The points of intersection of this line with those recording area an transverse diameter are then read off as representing the expected average area and with the addition of 10 per cent of the patient s age the expected average transverse diameter An allowance of 10 per cent extra is to be considered the extreme upper limi of normal (Kindness of Dr Chester M Kurtz Madison Wis)

Eyster 1924) Thus for a person fifty years old 173 cm (5 ft 8 in) tall and weighing 70 kg (154 lb) the orthodiagraphic cardiac area should be normally 112 sq cm If the heart area is found to be 7 sq cm larger than the predicted area by this formula the chances are 3 to 1 that the heart is actually enlarged if the actual area is 14 sq cm larger than the predicted area the chances of cardiac enlargement are 10 to 1 and if 21 sq cm larger the chances are 45 to 1 A simple calculation by slide rule or nomogram (Figure 29) can be made to determine the expected normal at any age height and weight for either orthodiagram or teleroentgenogram

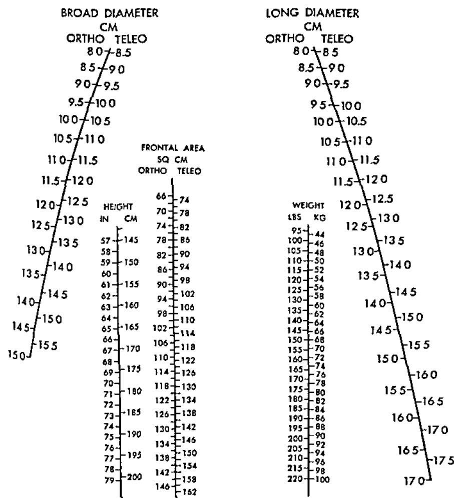


FIG 29B Area of heart shadow of orthodiagram and of teleroentgenogram determined from the long and broad diameters (the predicted area from height and weight) $A = \frac{\pi}{4} \times L \times B$ (Kindness of Dr Harry Ungerleider Equitable Life Assurance Society of the U.S New York City)

The ideal measurement of heart size by roentgen ray should be that of *volume* because of the established fact that the heart normally and abnormally varies considerably in all its diameters As yet however the determination of the heart volume has not been routinely introduced and under present condi tions it is not likely that it can be satisfactorily applied clinically for two rea sons (1) in the first place there is far too wide a range of normal heart size using recognized correlations and (2) the technic is not easy or accurate especially in the very cases of cardiac enlargement in which the physician is most interested Various formulas have been suggested especially those by Bardeen (1918) Kahlstorf (1932) Benedetti and Bollini (1934), and Strandquist (1935) Bardeen s formula is $0\ 53 \times A$ *(teleroentgenographic silhouette area)* $^{3/2} = V$ *(volume)* in a case with area of 100 sq cm the heart volume would be calculated to be 530 cc by this formula which is probabl not far from the true volume of a partially filled heart in an adult of averag size Kahlstorf's formula is V *(volume)* $= 0\ 63 \times$ *orthodiagraphic silhouett area of frontal plane heart shadow* $\times$ *maximum anteroposterior diameter* (D) If the area in a given case equals 100 sq cm and the anteroposterior diamete equal 8 5 cm the heart volume according to this formula would be 535 cc Benedetti and Bollini have published a formula for the tridimensional hear size Vc *(vol)* $= 0\ 45 \times$ *the long diameter of the heart in the anteroposterior orthodiagram* $\times$ *the broad diameter of the heart in the anteroposterior ortho diagram* $\times$ *the depth of the heart in the lateral orthodiagram* a case with lon diameter of 12 cm transverse diameter of 10 5 cm and depth of 9 cm woul thus have a volume of 510 cc Strandquist gives the following formula usin orthodiagraphic measurements V *(volume)* $= 2/3 \times 1/2\ L$ *(long diameter* $\times 1/2\ B$ *(broad diameter)* $\times S$ *(depth of heart in sagittal view)* using tele roentgenographic measurements he suggests $V = 0\ 42\ L \times B \times S$ Thus usin the last named formula in the case of a normal adult with L = 14 B = 1(and S = 9 we find that V = 529 cc One must of course correlate the hear volume determined by any formula to body size and also to the degree of fillin of the heart under some standard condition As has been noted already, th filling of the heart and hence its volume will vary greatly under certain con ditions probably changing at least 100 per cent in passing from the Valsalv experiment to the Muller experiment (see page 135)

Careful clinical studies made at the Massachusetts General Hospit (Comeau and White, 1939 and 1942) have demonstrated the inadequacy c all these various measurements chiefly because of the wide range of th normal heart size and shape in connection with all recognized correlation such as height and weight and body surface area It is hoped that other stand ards representing types of body build may some day prove more suitable an permit more reliance on roentgen measurements At present the simple trans verse diameter of the heart related to body height and weight followin Hodges and Eyster s tables seems the most satisfactory measurement of hear size with area a moderately close second The reason why area is not better a it should be on first thought is that a considerable part (the upper and lowe

borders) of the circumference of the heart shadow (in the anteroposterior view) has to be arbitrarily completed before the measurement by planimeter can be made This same reason plus the frequent difficulty of sharp measurement of the depth diameter of the heart (as well as the great range of normal) makes the volume calculation unsatisfactory The commonly used cardiothoracic ratio is in general too crude and its normal limits are far too wide however it can be useful in rare cases who are not tall but who have very wide chests

Finally it has been suggested that in addition to inspection of the size and density of the hilus shadows of the lungs in the anteroposterior heart shadow a measurement of their breadth be made This is much better done on the right side the measurement being actually that of the lower main branch of the right pulmonary artery Normally this hilus shadow measures 11 to 14 mm broad (average 13 mm) with the tube 1 5 meters away from thorax and screen If it is over 15 mm broad it is abnormal

Taken altogether these measurements of heart and aortic size should be interpreted very freely they are probably better than no measurements at all when they are so interpreted But when an attempt is made to fit each case within narrow so-called normal standard limits it is better to discard all measurements and to rely simply on general impressions and experience Some physicians do this now and are as successful in diagnosis as are other physicians who rely on extensive tables or formulas

Activity of the normal heart and great vessels as seen roentgenologically Normally the *atrial contractions* precede by a small fraction of a second (about 0 15 second) the contraction of the ventricles Theoretically this interval is sufficient to allow the atrial contractions to be visible in fluoroscopic examination but often this is not actually possible the vigorous ventricular action coming so soon after that of the atria that they both seem to share but a single motion If however the atria are enlarged and vigorous and very close attention is paid to the right atrial and left ventricular borders in the anteroposterior view or to the left atrial and left ventricular borders in the left anterior oblique view it is possible to distinguish a retraction of the atrial border ahead of the ventricular This separation becomes more and more obvious and marked with increasing delay in atrioventricular conduction and in complete block the atrial contractions may be clear Often atrial fibrillation weak or scant atrial contractions or obscure outlines prevent any evidence of atrial action at all in fluoroscopic examination and if there is free mitral or tricuspid regurgitation ventricular systole may be vigorous enough to cause an outward movement of the atrial borders

Ventricular action also varies very much normally in force extent and character In repose it tends to be quiet slight to moderate in fullness and slow with leisurely (that is relatively long) systole After exertion and with excitement it is active rapid and forceful with shorter systole with the especial increase of circulation due to exertion the contractions are fuller as well as more rapid In the upright position a vertical heart may beat rapidly and force-

fully laboring to send out blood which is coming to it in too small an amount Firm abdominal pressure by relieving this situation slows and calms the heart action When the ventricles contract apex and base of the heart approach each other the base moving down in this process even more than the apex moves up and the heart rotates to the right so that the apex of the left ventricle strikes the chest wall This composite movement is more obvious in the case of the horizontally placed heart than in that of the vertical heart It can be made more evident in either case by increasing the fullness of contraction by exercise The pulse of the ventricles is a single rapid process not accompanied by a wave of contraction the wave like change that is sometimes seen passing down over the base of the left ventricle with systole is simply the actual movement of the base that is the atrioventricular junction toward the apex as the heart contracts

The *great arteries* that is the aorta and pulmonary artery are seen to dilate with systole as the blood is pumped into them this results in a vertical rocking or seesaw motion of the heart shadow with retraction below and outthrust above especially evident along the left border This motion can be increased by exercise or excitement and in itself is not abnormal except as it may be much magnified under certain conditions as for example with aortic or pulmonary regurgitation Pulsation of the great veins is not normally visible except for that of the superior vena cava in the recumbent position when atrial and ventricular waves are seen A slight pendulous movement of the heart is due to respiration and not to heart action itself Moderate pulsation of the lung hiluses due to the presence there of the larger branches of the pulmonary artery may be normally visible in thin adults or in children with increased heart action

Roentgenkymography electrokymography and roentgencinematography already described above are methods that may be employed to obtain permanent records of cardiac and vascular pulsation and thus to supplement fluoroscopy

ABNORMALITIES OF SIZE SHAPE AND ACTIVITY OF HEART AND GREAT VESSELS STUDIED BY ROENTGEN RAY

The various abnormalities of the roentgen shadows of the heart and great vessels will be presented in appropriate chapters later in the book with particular relation to etiologic types and structural defect The index may be consulted for quick reference to the special pages concerned A few further notes should be added however in concluding the present chapter

Disorders of cardiac rhythm Although it is possible to diagnose such disorders of mechanism as premature beats paroxysmal tachycardia atrial fibrillation and even flutter atrioventricular nodal rhythm and heart block by fluoroscopy their identification and analysis are so much easier and more complete by other methods of examination especially electrocardiography that fluoroscopy is not a procedure of choice for their study Their presence may be first noted in roentgen ray examination but details are sure to be missed

With tachycardia whether of physiologic or pathologic nature the heart shadow often decreases in size with bradycardia the reverse is usually true

Calcification Calcification may be noted in *heart arteries* or *pericardium* It is most commonly and easily seen in the peripheral arteries especially in those of the legs The tortuous course of the calcified vessels may be found with or without symptoms or signs of faulty circulation in muscles and skin such as intermittent claudication or gangrene The next most common site of visible calcification is the thoracic aorta the whole vessel may be clearly out lined by general calcification (Figure 144 page 749) or there may be irregu larities of density due to plaques The abdominal aorta may also be sufficiently calcified to be visualized by roentgen ray especially if there is much air in the overlying gastrointestinal tract Uncommonly there may be enough cal cification of a diseased pericardium to be visible by roentgen ray (see Figure 140 page 730) such calcification is best noted end on in the oblique or lateral views Sometimes calcified valves (especially in calcareous aortic stenosis) or areas in the myocardium (old infarcts) or even calcified mural thrombi may be seen Calcified coronary arteries may be recorded on the roentgenogram or seen fluoroscopically but only in cases of advanced disease which is usually clearly evident on clinical examination here the cal cification is simply a gravestone covering tissue long dead

Pressure on bones Changes of bones due to erosion or deformity caused by heart or blood vessels are to be looked for A very large heart in early childhood may cause a bowing out of the left anterior chest wall With coarcta tion of the aorta the ribs may be eroded by the widened intercostal arteries a result of the attempt of the body to compensate for this congenital defect (see Figure 77 page 332) in some cases the diagnosis of this congenital defect has been first suggested by roentgen ray examination Vertebrae ster num and ribs may be found to be eroded by the pressure from aneurysms of thoracic or abdominal aorta or of the main branches of the thoracic aorta

Fat shadows At the apex there is often a considerable triangle of fat lying in a fold between pericardium pleura and diaphragm (epipericardial fat) this is of less density than the heart shadow (see text and Figure 7 pages 38 and 39) and should not be confused with it to occasion an incorrect diagnosis of cardiac enlargement such as has frequently happened (McGinn and White 1936) This mass of fat may be as wide in transverse diameter as 2 cm it can be easily differentiated on fluoroscopy especially on deep inspiration and by contrast films There may be fat also at the right heart border but of lesser amount

BIBLIOGRAPHY

CARDIOVASCULAR ROENTGENOLOGY

SEE ALSO REFERENCES UNDER CHAPTERS 23 OTHER ETIOLOGIC FACTORS AND RELATIONSHIPS 25 ABNORMALITIES OF MYOCARDIUM AND OF HEART CHAMBERS 26 VALVULAR DISEASE 27 PERICARDIAL DISEASE 28 VASCULAR DISEASE AND 34 HEART BLOCK

Assmann H *Die klinische Rontgendiagnostik der inneren Erkrankungen* F C W Vogel, Leipzig 4th ed 1928

Bardeen C R "Tables for Aid in the Determination of the Relative Size of the Heart by Means of the Roentgen Ray *Am J Roentgenol* 1917 IV 604

Determination of the Size of the Heart by Means of the X rays *Am J Anat* 1918 XXIII 423

Benedetti P and Bollini V Richerche cliniche sulla morfologia del cuore Nota seconda L ortocardiogramma in proiezione laterale e la determinazione del valore cardiaco *Endocrinol e pat cost t* Bologna 1934 IX 575

Bordet E and Fischgold H *La Radiokymographie du Coeur et des Vaisseaux* Masson et Cie Paris 1937

Castellanos A Pereiras R and Garcia A La Angio-cardiografia radio-opaca *Arch Soc estud clin Habana* 1937 XXXI Nos 9–10

Comeau W J and White P D An Evaluation of Heart Volume Determinations by the Rohrer Kahlstorf Formula as a Clinical Method of Measuring Heart Size *Am Heart J* 1939 XVII 158

Body Build and Heart Size Study of 20 Pairs of Identical Twins and 15 Pairs of Unrelated Individuals with Similar Body Height and Weight" *Am Heart J* 1939 XVII 616

A Critical Analysis of Standard Methods of Estimating Heart Size from Roentgen Measurements *Am J Roentgenol* 1942 XLVII 665

Crowden G P and Harris H A "The Effect of Obstructed Respiration on Heart and Lungs Its Clinical Importance in Radiography *Brit M J* 19_9 I 439

Danzer C S 'The Cardiothoracic Ratio An Index of Cardiac Enlargement" *Am J M Sc* 1919 CLVII 513

Dietlen H *Herz und Gefasse im Rontgenbild mit einem Beitrag uber Rontgenbefunde bei den Arhythmien des Herzens von A Weber* J A Barth Leipzig 1923

Edeiken J "A Comparison of the Orthodiagram with the Teleoroentgenogram *Am Heart J* 1940 XX 77

Gott T and Rosenthal J Ueber ein Verfahren zur Darstellung der Herzbewegung mittels Rontgenstrahlen (Rontgenkymographie) *Munch med Wchnschr* 1912 LIX 2033

Groedel F M *Die Rontgendiagnostik der Herz und Gefusserkrankungen* H Meusser Berlin 1912

Gubner R Crawford J H Smith W A and Ungerleider H E Roentgenkymography of the Heart Its Clinical Applications and Limitations *Am Heart J* 1939 XVIII 729

Hodges F J and Eyster J A E Estimation of Transverse Cardiac Diameter in Man *Arch Int Med* 1926 XXXVII 707

Hodges P C and Eyster J A E "Estimation of Cardiac Area in Man" *Am J Roentgenol* 1924 XII 252

Janker R "Roentgen Cinematography" *Am J Roentgenol* 1936 XXXVI 384

Kahlstorf A "Uber eine orthodiagraphische Herzvolumenbestimmung" *Fortschr a d Geb a Rontgenstr* 1932 XLV 123

"Uber Korrelationen der linearen Herzmasse und des Herzvolumens" *Klin Wchnschr* 1933 XII 262

Kohler A Die Herstellung fast orthodiagraphischer Herzphotogramme mittels Rontgeninstrumentarien mit kleiner Elektrizitatsquelle" *Wien klin Rundschau* 1905 XIX 279

Telerontgenographie des Herzens" *Deutsch med Wchnschr* 1908 XXXIV 186

Laubry C Cottenot, P Routier D and Heim de Balsac R *Radiologie clinique du Coeur et des gros Vaisseaux* Masson et Cie Paris 1939
Liljestrand G Lysholm E Nylin G and Zachrisson C G 'The Normal Heart Volume in Man *Am Heart J* 1939 XVII 406
McGinn S and White P D "Epipericardial Fat Its Nonrecognition a Common Cause of Error in X ray Measurement of Heart Size" *J.A.M A* 1936 CVII 200
Mazer M "A Simple Method for Measuring Cardiac Area from the Orthodiagram" *Am Heart J* 1942 XXIV 511
Moritz F "Ueber orthodiagraphische Untersuchungen am Herzen *Munch med Wchnschr* 1902 XLIX, 1
Palmer J H "The Development of Cardiac Enlargement in Disease of the Heart A Radiological Study" *Medical Research Council Special Report Series No 2??* His Majesty s Stationery Office London 1937
Palmieri G G "La radioplastique du coeur" *Arch d mal d coeur* 1921 XIV 440
Parkinson J and Bedford D E "The Aortic Triangle A Radiological Landmark in the Left (or II) Oblique Position *Lancet* 1936 II 909
Pezzi, C 'The Radioscopic Sign of the Hilum Dance Its Clinical Significance *Libman Anniversary Volumes* 1932 III 931
Reynolds R J "Some Experiments on the Production of Rapid Serial Roentgenograms from the Screen Image by Means of a Cinematographic Camera" *Brit J Radiol* 1927 XXIII 33 and *Am J Roentgenol* 1928 XIX 469
Cineradiography *Brit J Radiol* 1934 VII 415 and *Am J Roentgenol* 1935 XXXIII 522
Robb G P and Steinberg I "Practical Methods of Visualization of Chambers of the Heart the Pulmonary Circulation and the Great Blood Vessels in Man *J Clin Investigation* 1938 XVII 507 *Am J Roentgenol* 1939 XLI 1 and *J A M A* 1940 CXIV 474
Roesler H "Relation of Shape of Heart to Shape of Chest With Special Reference to Anteroposterior Dimension and Morphology of Various Normal Heart Types Contribution to Question of Accuracy of Ordinary Roentgenological Methods of Heart Measurement *Am J Roentgenol* 1934 XXXII 464
Clinical Roentgenology of the Cardiovascular System Charles C Thomas Publisher Springfield Ill 2nd ed 1943 (1st ed 1937)
Rohrer F Volumbestimmung von Koerpehoelen und Organen auf orthodiagraphischem Wege *Fortschr a d Geb d Rontgenstrahlen* 1916–17 XXIV 285
Rontgen, W K. Ueber eine neue Art von Strahlen" *Verhandl d physik med Gesellsch* Wurzburg, 1895 N F XXIX, 132
Sabat R Ueber ein Verfahren der rontgenographischen Darstellung der Bewegungen innerer Organe (des Herzens der Aorta des Zwerchfells) *Fortschr a d Geb d Rontgenst* 1913 XX 4?
Smith, H W and Bloedorn W A "The Size of the Normal Heart a Teleroentgen Study *U S Naval M Bull* 1922 XVI 219
Sosman M C 'Technic for Locating and Identifying Pericardial and Intracardiac Calcifications" *Am J Roentgenol* 1943 L 461
Spillane J D Volumetric Reconstruction of the Heart in Health and in Disease A Radiological Study" *Brit Heart J* 1939 I 333
Strandquist, M "Direction Indicator for Roentgen Tubes" *Acta radiol* 1935 XVI 304
Stumpf P "Archiv und Atlas der normalen und pathologischen Anatomie in typischen Rontgenbildern Das rontgenographische Bewegundsbild und seine Anwendung (Flachenkymographie und Kymoskopie)" *Fortschr a d Geb d Rontgenstrahlen* Erganzungsband 41 Georg Thieme Leipzig 1931
Ungerleider H E and Gubner R "Evaluation of Heart Size Measurements" *Am Heart J* 1942 XXIV 494
Valsalva A *De aure humana tractatus in quo integra auris fabrica multis novis inventis et iconismis illustrata describitur omniumque ejus partium uses indagantur Quibus interposita est musculorum uvulæ atque pharyngis nova descriptio et delineatio* Traj ad Rhenum G vande Water 1717
Vaquez, H and Bordet E *Radiologie du Coeur et des Vaisseaux de la Base* J B Bailliere et Fils Paris 4th ed 1928

Williams F H A Method for More Fully Determining the Outline of the Heart by Means of the Fluoroscope together with Other Uses of This Instrument in Medicine *Boston M and S J* 1896 CXXXV 335
Zdansky E Beitrage zur Kenntnis der kardialen Lungenstauung auf Grund rontgenologischer klinischer und anatomischer Untersuchungen *Wien Arch f inn Med* 1929 XVIII 461
Letter *J A M A* 1936 CVI 227
Rontgendiagnostik des Herzens und der grossen Gefasse Julius Springer Wien, 1939

Recent References (1944–1950)

Axen O and Lind J "Table for Routine Angiocardiography Synchronous Serial Roentgenography in Two Planes at Right Angles" *J A M A* 1950 CXLIII 540
Boone B R Gillick F G Chamberlain W E and Oppenheimer M J Electrokymograms of Heart Border Motion Principles of Record Interpretation *Federation Proc Fed of Am Soc for Exper Biol* 1946 V 9
Bustamente R Perez Stable E Guerra R and Milanés B Visualización radiologica de las arterias coronarias *Arch del Inst de cardiol de Mex* 1950 XX 350
Campbell M and Gardner F Radiological Features of Enlarged Bronchial Arteries *Brit Heart J* 1951 XII 183
Castellanos A and Pereiras R Retrograde or Counter Current Aortography *Am J Roentgenol* 1950 LXIII 559
Castellanos A Pereiras R and Garcia O Angio-cardiografia en el nino *Arch de Med Infantil Habana* 1950 XIX 29
Chavez I Dorbecker N and Celis A Direct Intracardiac Angiocardiography—Its Diagnostic Value *Am Heart J* 1947 XXXIII 560
Dotter C T and Steinberg M B "Angiocardiographic Interpretation *Radiology* 1949 LIII 513
Hanson H E Nyare erfarenheter med aortografi" *Nord med* 1949 XLI 55?
Henny G C and Boone B R Electrokymograph for Recording Heart Motion Utilizing the Roentgenoscope *Am J Roentgenol* 1945 LIV 217
Luisada A A Fleischner F G and Rappaport M B Fluorocardiography (Electrokymography) I Technical Aspects *Am Heart J* 1948 XXXV 336
McAllister F F and Beck C S A New X ray Technic for Visualization of the Heart and Great Vessels" *Circulation* 1950 I 1049
Meneses Hoyos J and Gomez del Campo C Angiographie de l aorte thoracique par ponction directe *Cardiologia* 1951 XVIII 156
Meyer R R A Method for Measuring Children s Hearts *Radiology* 1949 LIII 363
Prinzmetal M Corday E Bergman H C Schwartz L and Spritzler R J "Radiocardiography A New Method for Studying the Blood Flow Through the Chambers of the Heart in Human Beings *Science* 1948 CVIII 340
Ponsdomenech E R and Nunez V B "Heart Puncture in Man for Diodrast Visualization of the Ventricular Chambers and Great Arteries (I) Its Experimental and Anatomophysiological Basis and Its Technique and Heart Puncture (II) Cardioangiography Clinical and Electrocardiographic Results *Am Heart J* 1951 XLI, 643 and 855
Rushmer R F Cardiac Cinefluorography as a Training Method Abstract Program of 22nd Scientific Sessions Am Heart A 1949 p 44

CHAPTER 8

THE PULSATION OF HEART AND BLOOD VESSELS SPHYGMOGRAPHY BALLISTOCARDIOGRAPHY THE CAPILLARY CIRCULATION

Very little revision of this chapter has been needed for the present edition of this book A brief section however has been added on ballistocardiography for it is here that such mechanical recording belongs

Harvey W *Exercitatio Anatomica De Motu Cordis Et Sanguinis In Animalibus* Frankfurt am Main 1628 (*An Anatomical Disquisition on the Motion of the Heart and Blood in Animals* Translation by Robert Willis for the Sydenham Society in 1847)

Chapter I The Author s Motives for Writing

"When I first gave my mind to vivisections as a means of discovering the motions and us s of the heart and sought to discover these from actual inspection and not from the writings of others I found the task so truly arduous so full of difficulties that I was almost tempted to think with Fracastorius that the motion of the heart was only to be comprehended by God For I could neither rightly perceive at first when the systole and when the diastole took place nor when and where dilatation and contraction occurred by reason of the rapidity of the motion which in many animals is accomplished in the twinkling of an eye coming and going like a flash of lightning so that the systole presented itself to me now from this point now from that the diastole the same and then everything was reversed the motions occurring, as it seemed variously and confusedly together My mind was therefore greatly unsettled nor did I know what I should myself conclude nor what believe from others I was not surprised that Andreas Laurentius should have said that the motion of the heart was as perplexing as the flux and reflux of Euripus had appeared to Aristotle

"At length and by using greater and daily diligence having frequent recourse to vivisections employing a variety of animals for the purpose and collating numerous observations I thought that I had attained to the truth that I should extricate myself and escape from this labyrinth and that I had discovered what I so much desired both the motion and the use of the heart and arteries since which

Williams F H "A Method for More Fully Determining the Outline of the Heart by Means of the Fluoroscope together with Other Uses of This Instrument in Medicine *Boston M and S J* 1896 CXXXV 335

Zdansky E Beitrage zur Kenntnis der kardialen Lungenstauung auf Grund rontgenologischer klinischer und anatomischer Untersuchungen *Wien Arch f inn Med*, 19_9 XVIII 461

Letter *J A M A* 1936 CVI 227

R ntgendiagnostik des Her ens und der grossen Gefasse Julius Springer Wien, 1939

Recent References (1944–1950)

Axen O and Lind J "Table for Routine Angiocardiography Synchronous Serial Roentgenography in Two Planes at Right Angles *J A M A* 1950 CXLIII 540

Boone B R Gillick F G Chamberlain W E and Oppenheimer M J Electrokymograms of Heart Border Motion Principles of Record Interpretation *Federation Proc Fed of Am Soc for Exper Biol* 1946 V 9

Bustamente R Perez Stable E Guerra R and Milanés B "Visualización radiologica de las arterias coronarias *Arch del Inst de cardiol de Mex* 1950 XX 350

Campbell M and Gardner F Radiological Features of Enlarged Bronchial Arteries *Brit Heart J* 1951 XII 183

Castellanos A and Pereiras R Retrograde or Counter-Current Aortography" *Am J Roentgenol* 1950 LXIII 559

Castellanos A Pereiras R and Garcia O Angio-cardiografia en el nino" *Arch de Med Infantil Habana* 1950 XIX 29

Chavez I Dorbecker N and Celis A Direct Intracardiac Angiocardiography—Its Diagnostic Value *Am Heart J* 1947 XXXIII 560

Dotter C T and Steinberg M B "Angiocardiographic Interpretation *Radiology* 1949 LIII 513

Hanson H E Nyare erfarenheter med aortografi" *Nord med* 1949 XLI 55?

Henny G C and Boone B R Electrokymograph for Recording Heart Motion Using the Roentgenoscope *Am J Roentgenol* 1945 LIV 217

Luisada A A Fleischner F G and Rappaport M B Fluorocardiography (Electrokymography) I Technical Aspects" *Am Heart J* 1948 XXXV 336

McAllister F F and Beck C S A New X ray Technic for Visualization of the Heart and Great Vessels" *Circulation* 1950 I 1049

Meneses Hoyos J and Gomez del Campo C Angiographie de l aorte thoracique par ponction directe *Cardiologia* 1951 XVIII 156

Meyer R R A Method for Measuring Children s Hearts *Radiology* 1949 LIII 363

Prinzmetal M Corday E Bergman H C Schwartz L and Spritzler R J "Radiocardiography A New Method for Studying the Blood Flow Through the Chambers of the Heart in Human Beings *Science* 1948 CVIII 340

Pon domenech E R and Nunez V B Heart Puncture in Man for Diodrast Visualization of the Ventricular Chambers and Great Arteries (I) Its Experimental and Anatomophysiological Basis and Its Technique and Heart Puncture (II) Cardioangiography Clinical and Electrocardiographic Results *Am Heart J* 1951 XLI 643 and 855

Rushmer R F "Cardiac Cinefluorography as a Training Method Abstract Program of 22nd Scientific Sessions Am Heart A 1949 p 44

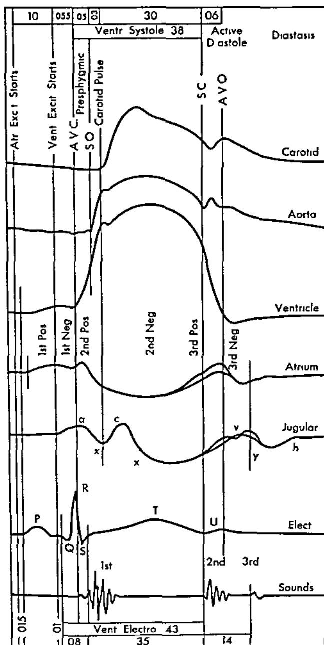


FIG 30 Chart showing time relations of electrocardiogram atrial and ventricular contractions pressure changes and heart sounds (Lewis *Mechanism and Graphic Registr tion of the Heart Beat* Kindness of Shaw and Sons Ltd London)

ence to the centre than in the opposite direction were there even no valves oppose its motion

Sphygmography (σφυγμος pulse and γραφειν to write) is the process obtaining a tracing of cardiovascular pulsation whether from the apex ir pulse of the heart (*cardiogram*) from brachial radial or other artery (*arter ogram*) from jugular or other vein (*phlebogram*) or from pulsating liv (*hepatogram*) The term polygram applies to simultaneous records of any tw or more pulses or of pulse and respiration Commonly the polygram registe the brachial or radial pulse and the jugular pulse in addition the electrocard ogram is usually recorded simultaneously or even replaces one of the oth mechanical graphic tracings The instrument which makes any of these cor bined tracings is called the polygraph The technic of sphygmography will n be discussed in this edition it is amply presented elsewhere (see Bibliograp at end of this chapter) It need only be added here that developments in tl last few years have made it possible to obtain with ease excellent electric (galvanometric) tracings of cardiac arterial and venous pulses (Miller ar White 1941) that total cardiac vibrations recorded by the cathode ray ai now available for study (Kountz and Smith 1941) and that graphic recor of the recoil of the body from the ejection of blood by the heart into the aor (ballistocardiograms) have been utilized to estimate the cardiac output p beat (Starr et al 1939 1940)

CARDIOGRAM

Although it may seem at first thought that records of the pulsation of th heart itself transmitted to the chest wall should be simple and reliable evidenc for the analysis of the mechanism of the heart beat experience has show otherwise The result is that the cardiogram is rarely obtained or studie except in special instances or in investigative work The reasons for this neg lect are several In the first place the technic is often far from easy A thic chest wall pulmonary emphysema or very weak heart action may make difficult or impossible to find any cardiac impulse at all In the second plac the shape and interpretation of the tracing depend on what part of the impuls is recorded whether that over the left ventricle at the apex or that nearer th sternum over the right ventricle In the third place the complexity of the trac ing which is often difficult to explain makes it less convenient than the arteri ogram phlebogram and electrocardiogram in the analysis of arrhythmias And finally in our present state of knowledge at least more helpful informa tion is afforded us by the other tracings for example slight pulsus alternans i the arteriogram shown poorly or not at all in the cardiogram delay in atrio ventricular conduction in the jugular phlebogram found with difficulty b direct cardiography and information about the myocardium shown by intra ventricular block and *T* wave changes of the electrocardiogram and usuall not even suggested by the cardiac apex tracing Nevertheless the cardiogram is of some individual interest for itself and should be briefly described

The normal cardiogram varies according to whether it is obtained over left ventricle or right ventricle (Figure 31) Over the left ventricle the outthrusts and hence the upstrokes of the tracing occur with systole over the right ventricle unless it is enlarged systole causes depression If the atrial contraction is vigorous and tracing conditions favorable we may find a definite upstroke a preceding the sharp higher ventricular upstroke of the left ventricular apex impulse or preceding in the same way the sharp ventricular downstroke over the right ventricle This a wave is more prominent over the right ventricle than over the left especially in the epigastrium A record taken where systolic outthrust and retraction merge will show various and sometimes confusing combinations of the two tracing shapes The wave due to ventricular contraction is usually overshot in the tracing partly because of the actual event but also because of the varying degrees of inertia of the apparatus employed Then follows during ventricular systole a settling down to a variable level till the shock of closure of aortic and pulmonary valves ends systole and begins diastole Quite early in diastole (about a tenth of a second after its onset) there may appear coincident with a protodiastolic heart sound a slight impulse due probably to the vibration of the ventricular walls from the current of blood that enters at that time (Figure 31) Such a diastolic event is more likely to be recorded with forceful slow heart action in thin young persons or with serious protodiastolic gallop rhythm (discussed in Chapter 5) Finally various oscillations may appear in the cardiogram which are unexplained but are probably due to vibrations of the chest wall

Abnormalities of the cardiogram include increased and decreased force and excursion of the atrial and ventricular systolic impulses and retractions delay between these impulses in heart block and extra waves in gallop rhythm (see Figure 31)

Gross pulsatory movements of the wall of the thorax resulting from the heartbeat (Dressler 1937) have already been referred to in Chapter 5 page 69

ARTERIOGRAM PULSE WAVE VELOCITY

Arteriogram An arterial pulse tracing may be obtained from almost any superficial artery but it is customary to use the brachial or radial artery for such a purpose Nearly a century ago the first attempts were made to study the circulation in man in health and disease by tracings on smoked paper made by crude instruments attached to the radial artery (Vierordt 1855 Marey 1860) Despite great expectations and extravagant interpretations the new records at first added little knowledge beyond that which had already been gained by mere palpation or inspection of the arterial pulse As a result sphygmography was abandoned for nearly half a century except for special studies The technic and apparatus poor and difficult at first slowly improved due to these special studies until with new discoveries concerning cardiac arrhythmia and alternation of the pulse the method was reintroduced into the clinic toward the end of the last century with far more success than at first

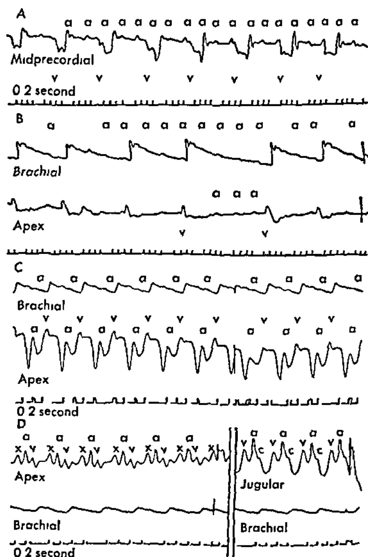


FIG 31 Cardiograms showing (*A*) ventricular systolic negative (v) and atrial systolic positive (a) waves in a case of complete heart block with the receiver placed over the precordium midway between the apex impulse and the lower end of the sternum and hence over the right ventricle (*B*) upstrokes with ventricular systole (v) and atrial systole (a) in the same case of complete heart block represented in (*A*) but with the receiver at the cardiac apex and hence over the left ventricle—note also the "a" waves in the brachial arteriogram taken simultaneously with the cardiogram (*C*) atrial (a) and ventricular (v) upstrokes with the receiver at the cardiac apex in a case with slight delay in a v conduction unusually vigorous atrial action and presystolic gallop rhythm and (*D*) three waves a v and x representing atrial ventricular and protodiastolic impulses with the receiver at the apex in a case of congestive failure showing well marked protodiastolic gallop rhythm without any delay in a v conduction (as proved by jugular phlebogram and electrocardiogram) Time interval = 0 2 second

It was almost entirely the shape and amplitude of the tracings that had attracted attention at the beginning rate and rhythm being largely ignored until many years later The various shapes of tracings of the arterial pulse were prominent in the textbooks of the day and it was hoped that they might prove more useful than they did We realize now that the shape and amplitude of the arteriogram are complicated not only in themselves but frequently also by the addition of artifacts due to the graphic method itself By the employment of more accurate apparatus the distortion can now be avoided

The normal arterial pulse wave The arteriogram consists of a graphic record of a series of pulse waves in an artery It should be of normal rhythm and rate (40 to 100 per minute at rest usually 60 to 80) The normal pulse wave (Figure 32) shows at first a sharp upstroke rising a variable distance from the baseline the amplitude depending on the fullness of the pulse and the sensitiveness of the recording apparatus Vibrations may be found on the upstroke if the curve is taken by the use of the Frank capsule crystal micro phone and galvanometer or cathode ray such vibrations are called anacrotic (ἀνα up and κροτο stroke) The upstroke is quickly succeeded by a short sharp fall to a notch called the predicrotic (προ before δις second and κροτο stroke) resulting from the artifact of overshooting or fling due to instrumental inertia The distance from the peak of the wave to the predicrotic notch varies according to two factors the amount of inertia of the recording apparatus and the fullness of the pulse the more of each of these the greater the distance It is not always possible to make out this notch it may be buried in the rapid decline to the dicrotic notch especially where there is a water hammer or hyperdicrotic pulse shape Following the predicrotic notch appears the curved systolic decline ending as a rule abruptly at the dicrotic notch which repre sents the time of aortic valve closure and second heart sound The time interval from beginning of the main upstroke to the dicrotic notch (usually 0 25 to 0 35 second depending on the pulse rate) represents the duration of systole minus the so-called presphygmic (προ before and σφυγμος pulse) interval which is the time at the beginning of systole after the closure of the mitral and tricuspid valves (time of first sound) when intraventricular pressure is rising but not sufficiently to raise the aortic cusps and start the pulse wave along the aorta this presphygmic interval or isometric (ἴσος equal and μετρον measure) phase is very short (calculated variously as 0 04 to 0 08 second) The dicrotic notch is followed by the dicrotic wave usually a slight convexity upward due to the rebound of the pulse wave at the closure of the aortic cusps This gives way to a gradual fall of the baseline to the next systolic upstroke Rarely a very small additional wave (a) occurs just preceding the systolic upstroke due to the effect of atrial systole on intraventricular and aortic pres sure Finally when more accurate tracings are obtained as already mentioned additional oscillations for example on the systolic upstroke may be seen doubtless due to vibrations of the artery wall their recording is not of any practical significance in the present state of our knowledge but may perhaps be found to be of some importance by future studies

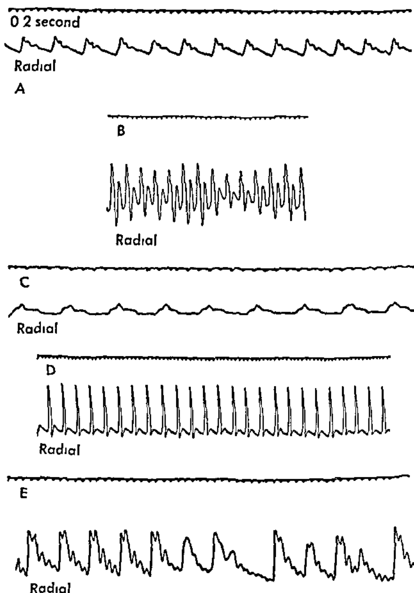


FIG 32 Arteriograms showing various shapes of pulse curves with normal rhythm (*A*) Normal average shape of arterial pulse wave showing upstroke predicrotic notch (due to artifact of overshooting from inertia of instrument) and dicrotic notch and wave (due to closure of aortic valve)—the duration of systole is equivalent to the interval from the beginning of the upstroke to the dicrotic notch plus a small time interval representing the presphygmic period (see text) (*B*) *Hyperdicrotic pulse in infection showing exaggeration of the dicrotic notch and wave* (*C*) Plateau and anacrotic pulse of aortic stenosis (*D*) Water hammer pulse of aortic regurgitation (*E*) Deformity of radial arteriogram due to oscillations caused by paralysis agitans Note also two ventricular premature beats Time interval of these and succeeding arteriograms and polygrams = 0 2 second

Abnormalities of the arterial pulse wave in shape and amplitude Slight changes in shape and amplitude of the arterial pulse wave from the average normal are so generally found in arteriograms or are so easily caused by the procedure of registration itself that only well marked variations such as can be palpated in the radial pulse should be considered here Great increase in pulse pressure that is true increase in artery fullness is not always easily apparent either on palpation of the arterial pulse or in the arteriogram Its detection is dependent on relative emptiness of the artery in diastole along with increase of pulse pressure but the diastolic laxness of the vessel is more essential than is increase in pulse pressure

Various abnormalities of shape and amplitude found in the arteriogram are illustrated in Figures 32 and 33

The most important by far of these abnormalities is *pulsus alternans* which consists of alternating fullness of pulse and of systolic and pulse pressure during normal heart rhythm the result of weakness (generally serious) of the left ventricle (see Chapter 30) An interesting variation abnormal and diagnostic (usually of acute or chronic constrictive pericarditis) when of high degree is the *pulsus paradoxus* which consists of waxing and waning of the pulse volume (and pressure) with expiration and inspiration respectively in contrast to the usual increase of the pulse fullness during inspiration and its decrease during expiration in the case of normal diaphragmatic breathing in marked instances the radial pulse may entirely disappear during inspiration (see Chapters 6 and 27) The various arrhythmias will not be illustrated here because they are so much better shown in electrocardiograms (see Chapters 32 33 and 34)

Velocity of the arterial pulse wave Quite aside from form and rhythm of the pulse and speed and volume of blood flow is the measurement of the velocity of the arterial pulse wave This has been estimated in various ways most simply by measuring the time interval between the appearances of the carotid and radial pulse waves graphically recorded simultaneously and dividing this time interval into the difference in centimeters between the distances from the heart of the recording points on the two arteries This gives roughly the speed of travel of the pulse wave in centimeters per second More accurate methods for making this measurement have been in recent years introduced such as that of the use of the hot wire sphygmograph which is an instrument transforming into variations of an electric current recorded by galvanometer the air pressure waves transmitted from a pulsating vessel or from the heart through a tube past a fine spiral of platinum wire heated by the electric current whose variations are recorded the ends of this wire being connected with the galvanometer Normally the pulse wave velocity in the brachial and radial arteries has been found to be 5 to 9 meters per second averaging about 7 meters It is increased in hypertension and arteriosclerosis and decreased in hypotension aortic stenosis and aortic aneurysm It varies roughly with the speed of blood flow but it has little or no relation

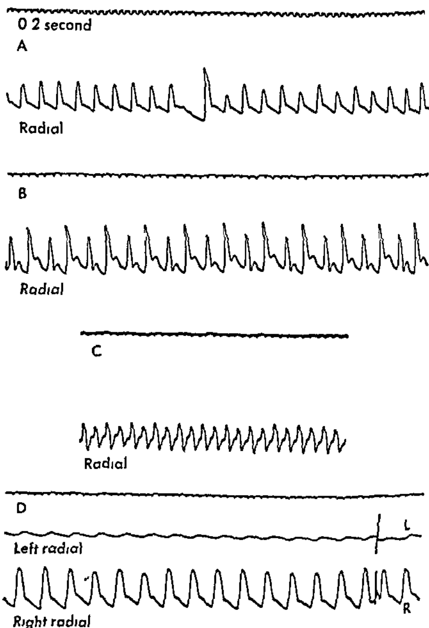


FIG 33 Arteriograms showing pulsus alternans and unilateral pulse deformity due to aneurysmal obstruction (*A*) Ventricular premature beat with compensatory pause followed by slight to moderate alternation of the pulse (*B*) Constant pulsus alternans showing delay in appearance of alternate weak beats (*C*) Pulsus alternans during paroxysm of tachycardia (rate 185 per minute) (*D*) Diminished and delayed left radial pulse waves due to aortic aneurysm with obstruction at the mouth of the left subclavian artery

to volume of blood flow The measurement of the velocity of the pulse wave is not of much clinical value

PHLEBOGRAM HEPATOGRAM

Phlebogram (φλέψ vein and γράμμα inscription) The phlebogram or graphic record of the venous pulse is routinely obtained from the jugular vein Although on rare occasions pulsations may be easily visible in other superficial veins as in the arms the jugulars as a rule are the only veins that show enough pulsation to give a satisfactory record this is due to their large size and close proximity to the heart Venous pulsation has been known for centuries but it was not until the latter half of the last century that the development of the sphygmograph permitted the taking of actual tracings (Friedreich 1866 Potain 1867) and serious study of these venous pulse tracings did not begin until stimulated by a curiosity concerning the clinical significance of variations of this pulse (Mackenzie 1893) Gradually by comparing the phlebogram thus obtained with cardiac or arterial pulse tracings it became possible to recognize although not completely to explain the various waves of the normal jugular pulse and to describe certain abnormalities

In the clinic for a while the analysis of disturbances of the cardiac mechanism like partial heart block was chiefly dependent on the study of the polygram which consisted of simultaneous jugular and arterial pulse tracings But the frequently difficult and bothersome technic and the obscurity concerning interpretation in the minds of most physicians prevented a wide adoption of the method doctors remaining content to continue for years the old custom of labeling irregularity of the heart rhythm as slight moderate or marked Eventually the interest of younger workers and especially the introduction of the practical electrocardiograph the string galvanometer into the field of internal medicine resulted in the clinical applications of the lessons about cardiac mechanism first studied in the phlebogram by pioneers The electrocardiogram gives information about the cardiac mechanism which is so much more accurate and complete than that given by the phlebogram and the technic of securing the electrocardiogram and its interpretation when obtained are both so much easier that the phlebogram has been almost completely abandoned However as in the case of the arteriogram help can still sometimes come from the phlebogram To represent graphically what one can see of jugular pulsation aids in understanding the mechanical evidences of cardiac action and is good training Also in certain cases when the electrocardiograph is not available and one deals with arrhythmias difficult to analyze without knowing how the atria are acting the phlebogram may solve the problem And even when an electrocardiogram has been secured the question as to whether atrial waves are isoelectric or buried in ventricular waves may be answered by a study of the phlebogram The jugular pulse tracing gives something the electrocardiogram cannot give that is mechani

cal evidence of action of the heart chambers moreover certain abnormalities of the jugular pulsation may reveal cardiac insufficiency even when the electrocardiogram is normal In addition one can by electrical recording now obtain phlebog ams with greater ease and accuracy than was possible in the past (Miller and White 1941)

The normal and abnormal jugular phlebogram Although proof does not exist for every detail of the interpretation of the normal jugular pulse tracing the phlebogram is understood sufficiently to permit fairly full analysis With each cardiac cycle there are normally three four five or even six waves in the jugular pulse Interpretation by inspection of these waves especially if there are more than three may prove to be very confusing Therefore although it is at times possible to see and to identify the three normal waves or in the case of abnormalities to make correct analyses there are so many variations that in spite of much experience interpretation by inspection of the vein is far less reliable than interpretation of the phlebogram itself

There are three main waves in the jugular pulse (Figure 34)

The first wave due to atrial systole, has been routinely called the *a* wave It can be identified only indirectly after the other two main waves (which are of ventricular origin) have been accurately measured off as a rule it precedes the second or *c* (ventricular systolic) wave by one fifth of a second and it is variable in size depending chiefly on the posture of the subject the force of the atrial contraction and the degree of dilatation of the jugular vein Other factors which influence the size of the *a* wave normally are instrumental technic and the fullness of blood flow With poor technic for example by the application of too much pressure so that the vein is nearly collapsed or by holding the receiver somewhat away from the optimum position the *a* wave of the phlebogram may be small and poorly defined With increased heart action the *a* usually increases in amplitude and with increased circulation associated with increased blood volume such as may temporarily result from the ingestion of a large amount of fluid the *a* wave may also increase in size It is biggest of all in cases of marked tricuspid stenosis with normal rhythm It is ordinarily a single wave a rounded upstroke rising sometimes at the peak of the jugular pulse sometimes low near the baseline and sometimes at midlevel its position depending on the speed of the pulse on the degree of stasis in the vein and on the relative submergence of the *a* in the ventricular systolic wave The slower the pulse or the more congested the vein the more the *a* wave tends to appear at the top of the curve The faster the pulse the less the congestion and especially the more the systole of the ventricles is emphasized in the tracing the lower lies the *a* wave Although the *a* wave appears normally to be a single wave this appearance may be in part due to the immediate succession of the ventricular systolic wave which conceals any other portion of the *a* wave When there is a delay in atrioventricular conduction partial or complete sufficient to separate clearly atrial and ventricular waves the *a* wave sometimes appears doubled

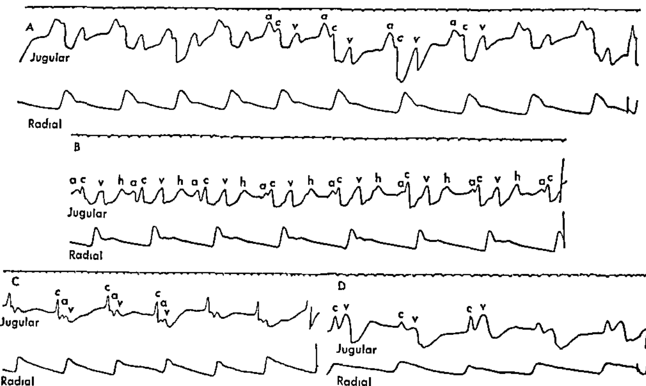


FIG 34 Polygrams showing the jugular phlebogram in (*A*) normal sinus arrhythmia (a = atrial c = ventricular and v = stasis waves) (*B*) sinoatrial bradycardia with h waves (see text) in addition to the a c and v waves (*C*) atrioventricular nodal rhythm in which the atrial contraction follows the ventricular as shown by the interpolation of the a wave between the c and v waves and (*D*) atrial standstill in which condition no a waves are seen either between or with the regularly recurring c and v waves

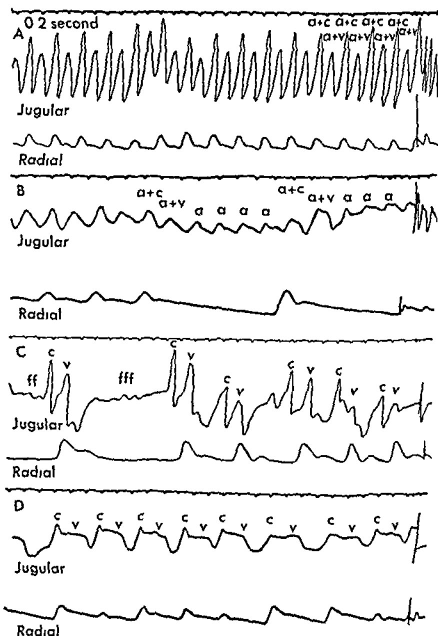


FIG 35 Polygrams showing the jugular phlebogram in (*A*) atrial flutter with two to one a v block (*a* = atrial *c* = ventricular and *v* = stasis waves) (*B*) atrial flutter with varying and higher degrees of block the *a* waves being clearly evident between the *c* waves (*C*) atrial fibrillation with no *a* waves but with oscillations (*fff*) due to the irregular atrial contractions and (*D*) atrial fibrillation with the so-called "ventricular or better designated "congestive" type of venous pulse due to coalescence of *c* and *v* waves resulting from stasis

or at least notched (Figure 36) Various abnormalities of the jugular phlebogram are illustrated in Figures 34 35 and 36 Arrhythmias are not presented because of their better analysis by electrocardiography (Chapters 32 33 and 34) except as they illustrate particular points concerning the venous pulse tracing

The a-c interval The atrial wave of the jugular pulse tracing precedes normally that due to ventricular systole by 0 15 to 0 20 second if there is a greater time interval (measured from the beginning of the *a* upstroke to the beginning of the *c* upstroke) atrioventricular block is present

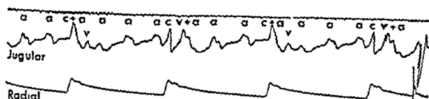


FIG 36 Polygram showing the jugular phlebogram in complete atrioventricular block with complete dissociation of *a* and *c* waves Note bifid *a* waves Size reduced

Following the first or *a* wave of the normal jugular phlebogram by the time interval just noted above appears the second or *c* wave which is due to ventricular systole It was labeled *c* because it was attributed to the pulsation of the carotid artery lying under the jugular vein Undoubtedly the carotid pulsation does play an important part in its production but this part is variable in degree In the venous pulsation itself there is a ventricular systolic wave transmitted up from the right atrium by way of the superior vena cava This wave together with that due to the carotid pulsation forms the upstroke *c* of the jugular phlebogram a positive wave of varying amplitude whose size depends upon a number of factors The greater the carotid element of the *c* wave the higher and more preponderant is this wave and vice versa There is one type of patient with mitral stenosis with greatly exaggerated *c* (and *v*) waves of the jugular pulse itself that deserves special mention This pulsation concerns the deep jugular veins on both sides of the neck but especially the right one Because as a rule atrial fibrillation is present in these patients with no *a* waves in the phlebogram because the pulse is so vigorous and because it is so deep in position in the neck it is easily and commonly confused with the carotid pulse (White and Cooke 1939) It is due to tricuspid regurgitation with relatively little constant congestion or stasis so that the pulse wave is propelled vigorously by right ventricular systole through tricuspid valve right atrium and superior vena cava into the jugular veins it is easily obliterated by slight pressure over the jugular bulb As a rule tricuspid valve deformity with stenosis is present in these cases of such pulsation of long standing but in rare instances there is chronic irreversible dilatation of the tricuspid ring without valve deformity

The *c* wave itself is identified by comparative measurement from the upstroke of the pulse wave of the brachial or radial arteriogram or of the *QRS*

wave of the electrocardiogram which is taken simultaneously with the jugula phlebogram for this very purpose Measuring back from simultaneous tim lines of both tracings established by allowing the pens each to write a strok with the recording surface at rest the beginning of the upstroke of the wave will be found one tenth of a second earlier than the upstroke of th radial pulse wave or 0 135 second later than the *QRS* wave this differenc in time being that interval required for the pulse wave to travel a length c artery equivalent to the difference between the distances of the radial puls and of the jugular pulse from the heart in the first instance and to the sur of the travel time from the heart to the jugular bulb and of the electrical pre sphygmic interval in the second instance (see Figure 31 page 158)

The *c* wave may be found to occur irregularly rapidly or slowly and t be of varying shapes and amplitudes but these characteristics of the arteri pulse and of heart action are better studied in the arteriogram itself as alread discussed or in the electrocardiogram

The third main wave the *v* wave of the jugular phlebogram is due pr marily to stasis that is to the gradual accumulation of blood in right atrium superior vena cava and jugular bulb at the close of ventricular systole Th stasis ends rather abruptly in a rounded peak and downstroke when diasto begins and the blood flows down into the right ventricle from atrium ven cava and jugular bulb It has been called routinely the *v* wave for ventricul systole but a more correct expression might have been *s* for stasis while the wave might better have been called the *v* wave However the firm stablisl ment and the partial correctness of these designations warrant their retentio A second factor besides stasis which has been suggested as in part responsib for the *v* wave is the rebound or return upward of the base of the heart at th beginning of diastole We do not know the relative importance of the tw elements (the rebound and the stasis) or whether the frequent splitting of th *v* wave which is unexplained can result from their difference in time (th diastolic rebound effect being later than the other) but evidence strongly sup ports the conclusion that stasis and not diastolic rebound is the essenti cause of the *v* wave The amplitude of the *v* wave varies as does that of the wave and as a rule inversely as that of the *c* wave It is dependent to an im portant degree on the amount of venous stasis If there is much stasis the wave is more prominent if the stasis is extreme in degree there appears characteristic variation consisting in a merging of *c* and *v* waves in one broa plateau with slight elevations at the ends and variable concavity between (Fig ure 35) This type of jugular pulse was once called the ventricular typ apparently because it was so often found in atrial fibrillation with absence c *a* waves But it may be found with normal rhythm and *a* waves It is due t congestion and so it may better be called the congestive type of jugula pulse

The *v* wave is determined in its position in the jugular phlebogram b correlation with the radial arteriogram simultaneously recorded Measurin back from synchronous points we find that the dicrotic notch of the arteri

pulse coincides with the peak of the v wave though sometimes it may fall between the two peaks of the v Actually the dicrotic notch of the radial pulse represents closure of the aortic valve an earlier event by 0 05 to 0 1 second than the opening of the tricuspid valve which is responsible for the beginning of the downstroke of the v wave But since the pulse wave takes almost 0 1 second longer to reach the wrist (or slightly less time to reach the elbow) than to reach the base of the neck these two events can be measured off together in the polygram

One further wave may be found infrequently in the jugular pulse tracing especially with slow forceful heart action It is a small wave in diastole called the *h* or *b* wave (Hirschfelder 1907 Gibson 1907) It is related to the preceding ventricular systole and not to the succeeding *a* or *c* waves which it may closely approach in time if the pulse is fast It has been ascribed to the same mechanism that produces the normal third sound of the heart or the abnormal extra sound in protodiastolic gallop rhythm but its timing sometimes appears late for this It is not well understood further study is needed to explain it Whatever its mechanism it does not at present appear important except that its existence should be recognized so that it will not be confused with other waves (Figure 34) The *a* and *h* waves are located by a process of exclusion after the *c* and *v* waves have been identified

What has been termed a second stasis or second onflow wave is the gradual movement upward of the baseline of the jugular phlebogram late in diastole just prior to the *a* wave it is prominent if there is bradycardia or congestion

An interesting phenomenon which sometimes interferes with smooth recording of the jugular pulse is the paradoxical inspiratory filling in cases of venous hypertension (Hitzig 1942) this has been discussed in Chapter 6 page 120 It emphasizes the need well known to those experienced in phlebography to obtain for their smoothness records taken during held respiration that is held in whatever phase brings out the pulse waves to the best advantage

An esophageal tracing of the left atrial pressure changes (esophagocardiogram) shows three waves usually corresponding to the *a* *c* and stasis waves of the jugular pulse tracing the *a* and *c* waves may be inverted if the receiver (a capsule filled with air) lies directly over the left atrium for the atrium recedes when it contracts as does the left ventricle This method however is an impracticable and unnecessary one

Hepatogram (ηπαρ liver and γραμμα inscription) A brief discussion of the liver pulse remains A true perceptible liver pulse not due to directly transmitted systolic movement of the liver by heart aorta or aneurysm is uncommon The reason for this is that the liver is so sponge like that it absorbs much blood and much pulsation before it becomes sufficiently influenced actually to cause a visible palpable or traceable pulse Slowly progressive *chronic pericarditis or heart failure although resulting in much* hepatic enlargement with some fibrotic change and ascites does not cause liver pulsation Three factors are responsible for this pulsation (1) rapid acute congestion with failure and functional tricuspid regurgitation (2)

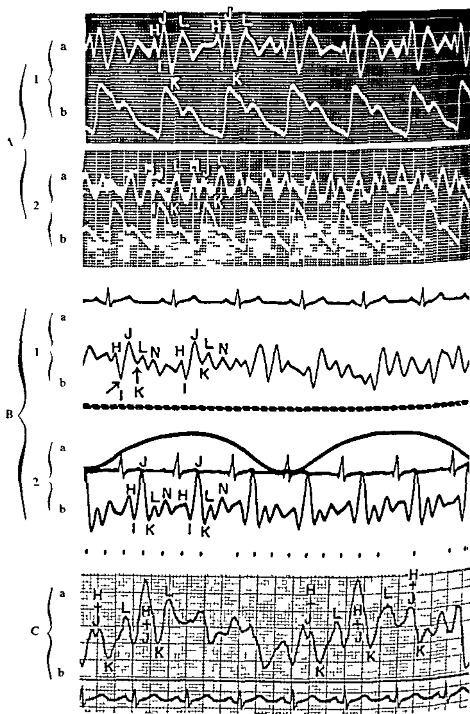


FIG 38 Ballistocardiograms (*A* 1) Normal curve Male age 34 Tracing shows normal waves H to K (period of cardiac ejection) Amplitude of J and K roughly approximate clinical measure of the stroke volume of the heart (*a* ballistocardiogram *b* arteriogram) (*A* 2) During acute rheumatic carditis The J and K waves are of

Rheocardiogram The changes that occur in the body s electrical resistance with each heartbeat can also be recorded electrically by connecting electrodes on right arm and left leg to alternating current of high frequency (10 000 to 50 000 oscillations per second) Measurement of electrical impedance of the body is not new in 1937 Mann stated When the electrical conductivity of any part of the body is measured by means of an alternating current bridge it is found that this conductivity shows a rhythmic variation synchronous with the pulse The curve which has been called an electrical plethysmogram ascends with increase in body resistance during systole when the heart volume decreases relative to the lung air volumes on either side and descends when diastole begins In myocardial failure with prolongation of the isometric period the descent of the curve is delayed and with mitral regurgitation the ascent is slowed (Holzer and Polzer 1947) Complete inversion of the curves has been reported in cases with extensive edema with reversal when the edema cleared (Weissel 1948) This technic has not however been adopted routinely in clinical practice further investigation is needed even to determine whether or not it has any value as a research tool Recent work has indicated its possible value in the study of the peripheral circulation (Nyboer 1950) where it may act as an electrically recording plethysmograph

CAPILLARY CIRCULATION AND PULSATION

It remained for Malpighi in 1661 to complete the proof of the circulation of the blood presented by Harvey in 1628 Harvey had postulated that "in the limbs and extreme parts of the body the blood passes either immediately by anastomosis from the arteries into the veins or mediately by the pores of the flesh, or in both ways as has already been said in speaking of the passage of the blood through the lungs Only in recent years has the existence of direct anastomoses between arteries and veins been demonstrated (Grant, 1931 Grant and Bland 1931) but the pores of the flesh or capillaries were discovered in the lungs by Malpighi.

Malpighi in a letter to Professor Alphonsus Borellius of Pisa describes his discovery of the pulmonary capillaries. (*De pulmonibus observationes anatomicae* Bologna 1661 translated by James Young M D *Proc Roy Soc Med* 1929–1930 XXIII 7–11 Part I)

low amplitude with relatively tall H and L waves (*a* ballistocardiogram *b* arteriogram) (Kindness of Dr William Dock Brooklyn, N Y)

(*B* 1) Ballistocardiogram and electrocardiogram of case of coarctation of aorta before operation showing relatively small J wave and very small K wave The arrows point to the short J and K strokes characteristic of coarctation of the aorta (*a* electrocardiogram *b* ballistocardiogram) (*B* 2) Same case after operation the J and K waves are now normal (*a* electrocardiogram *b* ballistocardiogram) (Kindness of Dr Herbert R Brown, Jr., Rochester N Y., and *New England J Med*)

(*C*) Case of angina pectoris, A D male age 49 Note respiratory effects but in particular the fusion and/or notching of the H and J waves (*a* ballistocardiogram *b* electrocardiogram) (Kindness of Dr William Dock, Brooklyn, N Y)

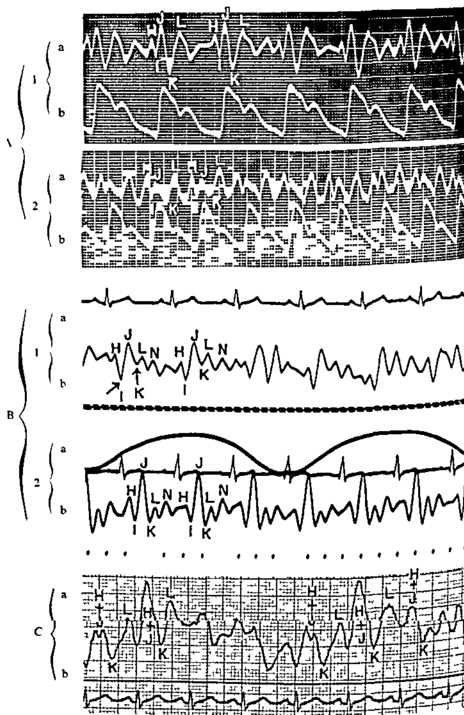


FIG 38 Ballistocardiograms (*A* 1) Normal curve Male age 34 Tracing sho
normal waves H to K (period of cardiac ejection) Amplitude of J and K rough
approximate clinical measure of the stroke volume of the heart (*a* ballistocardiogra
b arteriogram) (*A* 2) During acute rheumatic carditis The J and K waves are

Rheocardiogram The changes that occur in the body s electrical resistance with each heartbeat can also be recorded electrically by connecting electrodes on right arm and left leg to alternating current of high frequency (10 000 50 000 oscillations per second) Measurement of electrical impedance of the body is not new in 1937 Mann stated When the electrical conductivity of any part of the body is measured by means of an alternating current bridge it is found that this conductivity shows a rhythmic variation synchronous with the pulse The curve which has been called an electrical plethysmogram ascends with increase in body resistance during systole when the heart volume decreases relative to the lung air volumes on either side and descends when diastole begins In myocardial failure with prolongation of the isometric period the descent of the curve is delayed and with mitral regurgitation the ascent is slowed (Holzer and Polzer 1947) Complete inversion of the curves has been reported in cases with extensive edema with reversal when the edema cleared (Weissel 1948) This technic has not however been adopted routinely in clinical practice further investigation is needed even to determine whether or not it has any value as a research tool Recent work has indicated its possible value in the study of the peripheral circulation (Nyboer 1950) where it may act as an electrically recording plethysmograph

CAPILLARY CIRCULATION AND PULSATION

It remained for Malpighi in 1661 to complete the proof of the circulation of the blood presented by Harvey in 1628 Harvey had postulated that in the limbs and extreme parts of the body the blood passes either immediately by anastomosis from the arteries into the veins or mediately by the pores of the flesh or in both ways as has already been said in speaking of the passage of the blood through the lungs Only in recent years has the existence of direct anastomoses between arteries and veins been demonstrated (Grant 1931 Grant and Bland 1931) but the pores of the flesh or capillaries were discovered in the lungs by Malpighi

Malpighi in a letter to Professor Alphonsus Borellius of Pisa describes his discovery of the pulmonary capillaries (*De pulmonibus observationes anatomicae* Bologna 1661 translated by James Young M D *Proc Roy Soc Med* 1929–1930 XXIII 7–11 Part I)

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low amplitude with relatively tall H and L waves (*a* ballistocardiogram *b* arteriogram) (Kindness of Dr William Dock Brooklyn N Y)

(*B* 1) Ballistocardiogram and electrocardiogram of case of coarctation of aorta before operation showing relatively small J wave and very small K wave The arrows point to the short J and K strokes characteristic of coarctation of the aorta (*a* electrocardiogram *b* ballistocardiogram) (*B* 2) Same case after operation the J and K waves are now normal (*a* electrocardiogram *b* ballistocardiogram) (Kindness of Dr Herbert R Brown Jr Rochester N Y and *New England J Med*)

(C) Case of angina pectoris A D male age 49 Note respiratory effects but in particular the fusion and/or notching of the H and J waves (*a* ballistocardiogram *b* electrocardiogram) (Kindness of Dr William Dock Brooklyn N Y)

And now most famous man I will handle the matter more closely There were two things which in my epistle about observation on the lungs I left as doubtful and to be investigated with more exact study

(1) The first was what may be the network described therein where certain bladders and sinuses are bound together in a certain way in the lungs

(2) The other was whether the vessels of the lungs are connected by mutual anastomosis or gape into the common substance of the lungs and sinuses

The solution of these problems may prepare the way for greater things and will place the operations of Nature more clearly before the eyes For the unloosing of these knots I have destroyed almost the whole race of frogs which does not happen in that savage Batrachomyomachia of Homer For in the anatomy of frogs which by favour of my very excellent colleague D Carolo Fracassato I had set on foot in order to become more certain about the membranous substance of the lungs it happened to me to see such things that not undeservedly I can better make use of that (saying) of Homer for the present matter—

I see with my eyes a work trusty and great

For in this (frog anatomy) owing to the simplicity of the structure and the almost complete transparency of the vessels which admits the eye into the interior things are more clearly shown so that they will bring the light to other more obscure matters ——

Observation by means of the microscope will reveal more wonderful things than those viewed in regard to mere structure and connection for while the heart is still beating the contrary (i e in opposite directions in the different vessels) movement of the blood is observed in the vessels —though with difficulty—so that the circulation of the blood is clearly exposed This is more clearly recognized in the mesentery and in the other greater veins contained in the abdomen

Thus by this impulse the blood is driven in very small (streams) through the arteries like a flood into the several cells one or other branch clearly passing through or ending there Thus the blood much divided puts off its red colour and carried round in a winding way is poured out on all sides till at length it may reach the walls the angles and the absorbing branches of the veins

The power of the eye could not be extended further in the opened living animal hence I had believed that this body of the blood breaks into the empty space and is collected again by a gaping vessel and by the structure of the walls The tortuous and diffused motion of the blood in divers directions and its union at a determinate place offered a handle to this But the dried lung of the frog made my belief dubious This lung had by chance preserved the redness of the blood in (what afterwards proved to be) the smallest vessels where by means of a more perfect lens no more there met the eye the points forming the skin called Sagrino but vessels mingled annularly And so great is the divarication of these vessels as they go out here from a vein there from an artery that order is no longer preserved but a network appears made up of the prolongations of both vessels This network occupies not only the whole floor but extends also to the walls and is attached to the outgoing vessel as I could see with greater difficulty but more abundantly in the oblong lung of a tortoise which is similarly membranous and transparent Here it was clear to sense that the blood flows away through the tortuous vessels that it is not poured into spaces but always works through tubules and is dispersed by the multiplex winding of the vessels ——

Physiologic studies of the capillary circulation have in late years attracted much attention and have revealed new facts of some importance (Krogh Lewis Lombard Richards Crawford Landis) but in routine or even in special cardiovascular examination they have not yet proved important The reasons for this are two In the first place but few capillaries in man can be studied and these are at the body surface best seen at certain localities like the nail beds and subconjunctiva (and with difficulty in the eye grounds) In the second place great variations of capillary conditions exist not only throughout the body at a given moment but even in a single area at different moments due to the frequent periods of changing activity (dilatation) and rest (contraction) characteristic of arterioles and body capillaries in general Thus capillary findings at a given moment in a given area may be very different from those in many other areas or in the same area at a different time There are however certain clinical facts of interest determined by scrutiny of skin capillaries by microscope through the intervention of oil and the use of reflected light for illumination (Lombard 1912) In cyanotic states as in some cases of congenital heart disease with polycythemia or in one of the phases of Raynaud s disease capillaries of the fingers are widely dilated while the blood stream through them may be sluggish normal or rapid according to the state of the arterioles In conditions of pallor as in another phase of Raynaud s disease the capillaries and arterioles are constricted and the blood stream is slowed The ingenious studies by Crawford (1926 1927) and Landis (1930 1934 1938) have revealed interesting facts about the structure and action of the capillaries and concerning capillary blood pressure and permeability

Capillary pressure Landis (1930 1934 1938) by microinjection measured directly and studied the mean blood pressure in the capillaries of the human skin at the base of the finger nail He found the average pressure in the arteriolar limb of the capillary to be 32 mm of mercury at the end of the loop 20 mm and in the venous limb 12 mm The fall of blood pressure does not cease at the junction of the arterioles and capillaries he wrote but continues unbroken through the capillary loop Average blood pressure in the arteriolar limb is above and in the venous limb below the osmotic pressure of the plasma proteins These direct pressure readings in human capillaries are in agreement with Starling s hypothesis of fluid balance Landis further found that hyperemia due to heat was attended by a doubling of the capillary blood pressure Eichna and his associates (1942 1943) have shown that despite the fact that pressure in the capillaries of the digits falls somewhat with arteriolar constriction and rises somewhat with increase in venous pressure there is a surprising degree of constancy in the digital capillary pressure during wide fluctuations in digital blood flow Eichna (1943) reported his finding of the average digital capillary blood pressure in human fingers with intact innervation to be 18 5 mm of mercury in the arteriolar limb (summit 22 4) and 19 mm in the venous limb Recently Pappenheimer and Soto

Rivera (1948) have further confirmed the concept that capillary pressure and colloid osmotic pressure are in balance by measuring the rate of filtration of fluid from blood to tissues and absorption of fluid from tissues to blood in the isolated hindlimbs of cats and dogs under conditions such that the arterial perfusion pressure the venous pressure and the protein osmotic pressure could be independently adjusted to desired constant values

Capillary pulsation Capillary pulsation can be recorded only photographically by cinematograph under high power magnification With low power magnification pulsation in the smaller arteries would be predominant Visible capillary pulsation is due to vasodilatation or marked aortic regurgitation allowing the arterial pulse to enter the capillaries without adequate damping The site of the color change is in the subpapillary venous plexus (Lewis 1927) This capillary or venular pulsation may be general throughout the body or very local

BIBLIOGRAPHY

THE PULSATION OF HEART AND BLOOD VESSELS MECHANICAL RECORDS PULSE WAVE VELOCITY BALLISTOCARDIOGRAPHY CAPILLARY CIRCULATION AND PULSATION

SEE ALSO GENERAL REFERENCES FOLLOWING CHAPTER 2 AND IN PART IV DISORDERS OF CARDIOVASCULAR FUNCTION

Bazett H C and Dreyer N B "Measurements of Pulse Wave Velocity" *Am J Physiol* 192? LXIII 94

Dressler W Pulsations of the Wall of the Chest *Arch Int Med* 1937 LX ? ? 437 441 654 and 663

Ewing E M 'The Venous Pulse *Am J Physiol* 1914 XXXIII 159

François Franck Mouvement des veines du cou en rapport avec l action de la respiration et du coeur *Ga hebd d méd et d chir* 1882 pp 132 156 225 and 255

Frank O Dynamik der Membranmanometer und der Lufttransmission" *Ztschr f Biol* 1907–8 L 309

Friedreich N Ueber den Venenpuls *Deutsch Arch f klin Med* 1866 I ?41

Gibson, A G The Significance of a Hitherto Undescribed Wave in the Jugular Pulse *Lancet* 1907 II 1380

Harvey W *Exercitatio Anatomica De Motu Cordis Et Sanguinis in Animalibus* Frankfurt am Main 1628

Hirschfelder A D "Some Variations in the Form of the Venous Pulse *Bull Johns Hopkins Hosp* 1907 XVIII 265

Hitzig W M On Mechanisms of Inspiratory Filling of the Cervical Veins and Pulsus Paradoxus in Venous Hypertension *J Mt Sinai Hosp* 1942 VIII 625

Holzer W and Polzer K Rheokardiographie ein neues Kreislaufuntersuchungsverfahren *Schweiz med Wchnschr* 1947 LXXVII 921

Kountz, W B and Smith J B "Total Cardiac Vibrations Recorded by the Cathode Ray *Soc Proc J Clin Investigation* 1941 XX 458

Lancisi G M *De Motu Cordis et Aneurysmatibus* Rome 1728

Lewis T *The Mechanism and Graphic Registration of the Heart Beat* Shaw & Sons Ltd London 3rd ed 1925 (1st ed 1911)

Mackenzie J "Pulsations in the Veins with the Description of a Method for Graphically Recording Them" *J Path & Bact* 1893 I 53

The Study of the Pulse Arterial Venous and Hepatic and of the Movements of the Heart Macmillan Co New York and London 1902

"The Ink Polygraph" *Brit M J* 1908 I 1411

Mann H Study of Peripheral Circulation by Means of an Alternating Current Bridge" *Proc Soc Exper Biol & Med* 1937 XXXVI 670
Marey E J Recherches sur l etat de la circulation d après les caracteres du pouls fournis par un nouveau sphygmographe *J de la physiol de l homme* Paris 1860 III 241
Miller A and White P D Crystal Microphone for Pulse Wave Recording" *Am Heart J* 1941 XXI 504
Morgagni J B *De Sedibus et Causis Morborum* Ex typog Remondiniani Venice 1761
Nyboer J Electrical Impedance Plethysmography A Physical and Physiologic Approach to Peripheral Vascular Study" *Circulation* 1950 II 811
Potain P C E Des mouvements et des bruits qui se passent dans les veines jugulaires *Bull et mem Soc méd d hop d Paris* 1867 IV 2eme serie pp 3-27 of the *Memoires* of the Society
Puddu V Rheumatic Heart Disease with Normal Rhythm and Very Large a Waves in the Jugular Pulse" *Am Heart J* 1951 XLI 708
Taquini A C "The Esophageal Pulse under Normal and Abnormal Conditions *Am Heart J* 1940 XX 129
Vierodt, K *Die Lehre von Arterienpuls in gesunden und kranken Zustanden* Friedrich Vieweg und Sohn Braunschweig 1855
Weissel W Die Inversion des Rheokardiogramms zugleich ein Beitrag zur Kenntnis der extracardialen Beeinflussbarkeit der Kurve *Wien Ztschr fur Inn Med und ihre Grenzgebiete* 1948 XXIX 341
Wenckebach K F *Die Arhythmie als Ausdruck bestimmter Funktionsstorungen des Herzens* W Engelmann Leipzig 1903
White P D and Cooke W T "The Recognition and Significance of Marked and Chronic Systolic Pulsation of the Deep Jugular Veins *Tr A Am Physicians* 1939 LIV 199

Ballistocardiography

Abramson E "Die Ruckstosskurve des Herzens (Kardiodynamogramm) *Skandinav Arch f Physiol* 1933 LXVI 191
Brown H R Jr Hoffman M J and deLalla V Jr Ballistocardiograms in Coarctation of the Aorta *New England J Med* 1949 CCXL 715
Cournand A Ranges H A and Riley R L Comparison of the Results of the Normal Ballistocardiogram and a Direct Fick Method in Measuring the Cardiac Output in Man *J Clin Investigation* 1942 XXI 287
Dock W and Taubman F Some Technics for Recording the Ballistocardiogram Directly from the Body *Am J Med* 1949 VII 751
Dow P and Hamilton W F An Analysis by Hydraulic Models of the Factors Operating to Produce the Typical Ballistocardiogram *Am J Physiol* 1941 CXXXIII 263
Gordon J W "Certain Molar Movements of the Human Body Produced by the Circulation of the Blood. *J Anat & Physiol* 1877 XI 533
Hamilton W F and Dow P Cardiac and Aortic Contributions to the Human Ballistocardiogram *Am J Physiol* 1941 CXXXIII 313
Hamilton W F Dow P and Remington J W The Relationship Between the Cardiac Ejection Curve and the Ballistocardiographic Forces *Am J Physiol* 1945 CXLIV 557
Henderson Y "The Mass Movements of the Circulation as Shown by a Recoil Curve *Am J Physiol* 1905 XIV 287
Krahl V E "The Electric Strain Gauge Ballistocardiograph *Am Heart J* 1950 XXXIX 161
Mathers J A L Nickerson J L Fleming T C and Patterson M C Abnormal Ballistocardiographic Patterns in Cardiovascular Disease as Recorded with the Low Frequency Critically Damped Ballistocardiograph *Am Heart J* 1950 XL 390
Nickerson J L The Ballistocardiographic Pattern with Special Reference to the H Wave *Am Heart J* 1949 XXXVII 656
Nickerson J L and Curtis H J "Design of Ballistocardiograph *Am J Physiol* 1944 CXLII 1
Starr I and Mayock R L On the Significance of Abnormal Forms of the Ballisto-

cardiogram A Study of 234 Cases with 40 Necropsies" *Am J M Sc* 1948 CCXV 631
Starr I Rawson A J Schroeder H A and Joseph N R "Studies on the Estimation of Cardiac Output in Man and of Abnormalities in Cardiac Function, from the Heart s Recoil and the Blood s Impacts the Ballistocardiogram *Am J Physiol* 1939 CXXVII 1
Starr I, and Schroeder H A Ballistocardiogram II Normal Standards Abnormalities Commonly Found in Diseases of the Heart and Circulation and Their Significance *J Clin Investigation* 1940 XIX 437
Wilkins R W A Tilting Ballistocardiograph *Am Heart J* 1943 XXVI 351

Capillary Circulation and Pulsation

Crawford J H and Rosenberger H "Studies on Human Capillaries I An Apparatus for Cinematographic Observation of Human Capillaries *J Clin Investigation* 1926, II 343
II Observations on the Capillary Circulation in Normal Subjects *Ibid* p 351
III Observations in Cases of Auricular Fibrillation *Ibid* p 365
Danzer C S and Hooker D R "Determination of the Capillary Blood Pressure in Man with the Microcapillary Tonometer *Am J Physiol* 1920 LII 136
Eichna L W Capillary Blood Pressure in Man Direct Measurements in the Digits During Arterial Hypertension Induced by Paredrinol Sulfate" *J Clin Investigation* 1942 XXI 731
Capillary Blood Pressure in Man Direct Measurements in the Digits of Patients with Raynaud s Disease and Scleroderma Before and After Sympathectomy *Am Heart J* 1943 XXV 812
Eichna L W and Bordley J III Capillary Blood Pressure in Man Comparison of Direct and Indirect Methods of Measurement *J Clin Investigation* 1939 XVIII 695
Capillary Blood Pressure in Man Direct Measurements in the Digits of Normal and Hypertensive Subjects during Vasoconstriction and Vasodilatation Variously Induced *Ibid* 1942 XXI 711
Grant R T Observations on Direct Communications Between Arteries and Veins in the Rabbit s Ear *Heart* 1930-31 XV 281
Grant R T and Bland F F Observations on Arteriovenous Anastomoses in Human Skin and in the Bird s Foot with Special Reference to the Reaction to Cold." *Heart* 1931 XV 385
Krogh A *The Anatomy and Physiology of Capillaries* Yale University Press New Haven 2nd ed 1929 (1st ed 1922)
Landis E M Micro Injection Studies of Capillary Blood Pressure in Human Skin *Heart* 1930 XV 209
Capillary Pressure and Capillary Permeability *Physiol Rev* 1934 XIV 404
"The Capillaries of the Skin Review" *J Invest Dermat* 1938 I 295
Lewis T *The Blood Vessels of the Human Skin and Their Responses* Shaw & Sons Ltd London 1927
Lombard W P The Blood Pressure in the Arterioles Capillaries and Small Veins of the Human Skin *Am J Physiol* 1911-12 XXIX 335
Malpighi M *De pulmonibus observationes anatomicae* Bologna 1661
Pappenheimer J R and Soto-Rivera A "Effective Osmotic Pressure of the Plasma Proteins and Other Quantities Associated with the Capillary Circulation in the Hindlimbs of Cats and Dogs *Am J Physiol* 1948 CLII 471
Richards A N and Schmidt C F "A Description of the Glomerular Circulation in the Frog s Kidney and Observations Concerning the Action of Adrenalin and Various Other Substances Upon It" *Am J Physiol* 1924 LXXI 178

CHAPTER 9

ELECTROCARDIOGRAPHY

One of the interesting medical achievements of our time has been the rapid indeed one might say dramatic growth of electrocardiography (ἤλεκτρον amber friction of which gives rise to an electrical charge καρδια heart and γράφειν to write) To those of us who received our initial training in this field in the early days of clinical electrocardiography this evolution has been both gratifying and impressive not to say at times confusing The confusion has been due to two factors first the absence at the beginning of an adequate application of fundamental physical laws and principles so that the early growth was more empirical than scientific and second the lack of uniform technic and nomenclature utilized by various workers in the field This vigorous independence of thought and action has however its good side and agreement about utilization of the most satisfactory viewpoints and criteria will naturally follow We are still in the very midst of considerable new research and development in electrocardiography It would be impossible for me in the limited space available in this new edition to expand the chapter sufficiently to present the subject in all of its current detail I shall retain the story of the evolution of clinical electrocardiography with a brief survey of its present status and refer the reader for a more complete description of technic debatable theories and current research to the numerous monographs now available and listed in the Bibliography at the end of the chapter

Electrocardiography is one of the most important methods of cardiovascular examination ranking in value third after history taking and physical examination Like cardiovascular roentgenology it has continued to develop rapidly as the result of concentrated study in the past decades

Near the end of the eighteenth century Galvani and Volta and their followers began their important studies on electricity by utilizing that produced by animals Galvani for example in 1791 used the electrical organ of the torpedo-fish to stimulate not only the muscles and nerves of the frog but also the heart itself

About the middle of the last century it was learned in the exp

laboratory that when the pigeon s or the frog s heart contracted it produced an electric current (Matteucci 1843 Kolliker and Muller 1856) For many years after this discovery the heart current of laboratory animals was studied with the crude apparatus at that time available

Matteucci Ch Sur le courant électrique des muscles des animaux vivants ou recemment tues *Comptes Rendus des Seances de l Academie des Sciences* 1843 XVI 197

1 The signs of the electrical current of the frog itself demonstrated by the galvanometer increase in the same instrument in the act of contraction

2 *The muscular electrical current* which I shall hereafter call the muscular current is present in all muscle masses whatever the animal

I have taken pectoral muscles of pigeons a rabbit s back muscles hearts of pigeons In all cases I have obtained a current which flows from the interior of the muscle to the surface (Translation by myself)

Kolliker A and Muller H Nachweis der negativen Schwankung des Muskel stroms am naturlich sich contrahirenden Muskel *Verhandlungen der phy sicalisch medicinischen Gesellschaft in Wurzburg 1856 VI 528*

The results which up to now we have obtained from the frog s heart are as follows

1 The apex of the whole heart is electrically negative to any point on the anterior or posterior surface of the ventricles

2 Similarly negative is the apex of the heart to the cut surfaces left after removing the auricles without injury to the ventricles

3 On the other hand the cardiac apex is positive to any cross section which involves the ventricular musculature itself

4 Every point on the surface of the heart is positive to any selected cross section of the ventricle

5 The excursion given by connecting the outer surfaces of the base and of the apex of the heart is less than that given by connecting the cross section of the apex and the surface (Translation by myself)

Then came the discovery six decades ago also in the physiologic laboratory that the human heart current could be demonstrated by connecting the outside of the body by electrodes with the capillary electrometer (Waller 1887)

Waller A D A Demonstration on Man of Electromotive Changes Accompanying the Heart s Beat *J Physiol* 1887 VIII 229

If a pair of electrodes (zinc covered by chamois leather and moistened with brine) are strapped to the front and back of the chest and connected with a Lippmann s capillary electrometer the mercury in the latter will be seen to move slightly but sharply at each beat of the heart If the movements of the column of mercury are photographed on a travelling plate simultaneously with those of an ordinary cardiographic lever a record is obtained as under (fig 1) in which the upper line h h indicates the heart s movements and the lower line l l the level of the mercury in the capillary Each beat of the heart is seen to be accompanied by an electrical variation [This very first published electrocardiogram is essentially

the chest lead reintroduced as Lead 4 into clinical electrocardiography in recent years]

The first and chief point to determine is whether or no the electrical variation is physiological and not due to mechanical alteration of contact between the electrodes and the chest wall caused by the heart s impulse To ascertain this point accurate time measurements are necessary a physiological variation should precede the movement of the heart while this could not be the case if the variation were due to altered contact Fig 2 is an instance of such time measurements taken at as high a speed of the travelling surface as may be used without rendering the initial points of the curves too indeterminate It shows that the electrical phenomenon begins a little before the cardiographic lever begins to rise

That a true electrical variation of the human heart is demonstrable may further be proved beyond doubt by leading off from the body otherwise than from the chest wall If the two hands or one hand and one foot be plunged into two dishes of salt solution connected with the two sides of the electrometer the column of mercury will be seen to move at each beat of the heart though less than when the electrodes are strapped to the chest The hand and foot act in this case as leading off electrodes from the heart and by taking simultaneous records of these movements of the mercury and of the movements of the heart it is seen that the former correspond with the latter slightly preceding them and not succeeding them as would be the case if they depended upon pulsation in the hand or foot This is unquestionable proof that the variation is physiological for there is here no possibility of altered contact at the chest wall and any mechanical alteration by arterial pulsation could only produce an effect 0 15" to 0 20 after the cardiac impulse A similar result is obtained if an electrode be placed in the mouth while one of the extremities serves as the other leading off electrode The electrical variation precedes the heart s beat as in the other cases mentioned

The mercury column moved up and down several times with each heartbeat but the records obtained by photographing its shadow were inaccurate because of the inertia of the instrument Laboriously the electric heart tracings or electrocardiograms were obtained and corrected and considerable progress in their analysis was made by physiologists at the end of the last century (Bayliss and Starling 1892) and at the beginning of the present century Finally in 1903 came the announcement of the invention of the accurate and practicable string galvanometer (Einthoven) a few years later this was introduced into hospitals and clinical electrocardiography began

Einthoven W Die galvanometrische Registrirung des menschlichen Elektrokardiogramms zugleich eine Beurtheilung der Anwendung des Capillar Elektrometers in der Physiologie *Pfluger's Arch f d ges Physiol* 1903 XCIX 472

(Page 474) I have tried to find a way to avoid as far as possible the construction of a new curve [that is a corrected curve such as it was necessary to construct in the use of the capillary electrometer] in so doing I have at length devised an instrument which satisfies many requirements and is especially suitable to inscribe the human electrocardiogram directly in almost its exact proportions

The essential part of this instrument—the string galvanometer—is a thin silver coated quartz fibre which is stretched like a string in a strong magnetic field If

an electric current is led through this quartz fibre the fibre shows a movement which can be observed and photographed by means of considerable magnification, just as is the case with the movement of the mercury in the capillary electrometer It is possible to regulate the sensitivity of the galvanometer very accurately within wide bounds by tightening and loosening the string (Translation by myself)

During the past three decades with the development of audion tube amplification the dead beat mirror galvanometer has been adapted to clinical electrocardiography and is the basis for much of the easily portable apparatus that can be carried to the sickroom for cardiac registration of patients at home in bed The cathode ray has also been utilized to record the electrical activity and sounds of the heart in man but it is unnecessarily expensive in cost and in the use of high operating voltage for the needs of clinical electrocardiography and phonocardiography although in current research it is being utilized with extensive chest leads to explore details of the course of electrical discharge and repolarization through the heart muscle (Goldman) *

A recent innovation has been the utilization of an ingenious device of a heated stylus which activated by a galvanometer moves without friction or overshooting over the surface of a moving processed (wax covered) paper strip to inscribe the electrocardiogram directly without the trouble time and expense of photographic technic This type of direct writing electrocardiograph has the advantage of accuracy in recording over the initial ink writing galvanometers which were originally introduced to simplify the clinical technic

At first electrocardiography was sought and used chiefly as an aid in the explanation of cardiac arrhythmia tachycardia and bradycardia having proved to be more satisfactory than the mechanical graphic methods previously employed because of the greater ease of technic and interpretation and because of the more complete information afforded As time went on however it was learned that more important data about the heart than the explanation of abnormalities of rate and rhythm are shown by the electrocardiogram from a study of the shape direction amplitude and time relations of the individual waves or deflections especially as they are compared in various leads

It is unfortunate that we do not even as yet know the range of the normal electrocardiogram it is wider than we thought it was ten years ago and much service can still be wrought by the simple electrocardiographic analysis of many thousands of normal individuals It is also important to become familiar with the electrocardiogram in infancy which is different from that in older children and adults not only in much faster heart rate but in much narrower time intervals especially *P R* interval and *QRS* duration (shorter by one third to one half—see Figure 54 page 214) and in its normal right axis deviation It is interesting that the human infant s type of electrocardiogram becomes recognizable at the end of the first month of fetal life (Marcel and

* Recently cathode ray electrocardiography by radio (remote control) has been introduced by Holter of Helena Montana (1949) and by Kanatsoulis of Athens Greece (1950)

Exchaquet 1938) also exploration of the maternal abdomen to obtain fetal electrocardiograms has been found successful in 85 to 90 per cent of cases (Goodyear et al 1942)

The electrocardiograph does not take the place of such other methods of examination as history taking percussion auscultation and roentgenology but it does obviate in large part the need of taking mechanical graphic records of arterial and venous pulses and of the apex impulse *Finally it must be realized that the electrocardiogram may be perfectly normal even in the presence of serious heart disease* This method of study should therefore be viewed modestly as helpful but not accorded too great importance

The electrocardiogram itself is written by the spread of electrical activity that sweeps down the heart from its pacemaker at each heartbeat in peristaltic waves over the atria and by special conduction tracts and fibers into the ventricles (Figure 39)

It is the movement of the string shadow or beam of light that causes the waves (usually called deflections or complexes) of the electrocardiogram

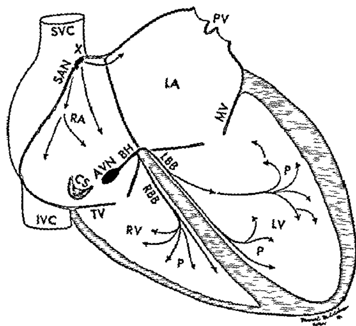


FIG 39 Diagram of excitatory and conduction system of the heart

SVC superior vena cava
IVC inferior vena cava
RA right atrium
CS coronary sinus
TV tricuspid valve
RV right ventricle
PV pulmonary veins
LA left atrium
MV mitral valve
LV left ventricle
SAN sinoatrial node
X usual site of pacemaker
AVN atrioventricular node
BH bundle of His
RBB right bundle branch
LBB left bundle branch
P Purkinje network radiating out from papillary muscles

(Graybiel and White s *Electrocardiography in Practice* W B Saunders C Philadelphia)

These waves chiefly three have been variously named The German school at first labeled them *a* for atrial wave *i* for the first or initial ventricular wave and *f* for the second or final ventricular wave these designations have been justified by time but they have not been generally adopted Einthoven s letters arbitrarily taken from the middle of the alphabet and attached to the deflections so as not to prejudice future workers in the study of the cardiac mechanism have become universally employed and will be used here the first deflection or atrial wave is called *P* the second deflection or the first ventricular wave a rapid succession of one two or three deflections is called *Q R* and *S* and the third deflection or second ventricular wave is called *T* (Figure 40) There is often a small final and unexplained wave called *U*

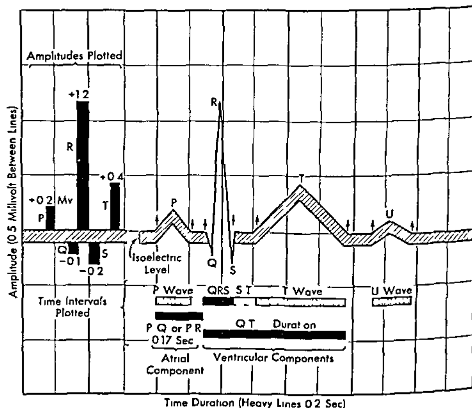


FIG 40 Diagram of normal electrocardiogram showing the individual complexes with special reference to amplitude and time duration *P* = atrial deflection *QRS* = first ventricular deflection *ST* segment and *T* wave = remainder of ventricular activity beginning of *Q* to end of *T* = duration of systole

There are two essential methods of description of the normal and abnormal electrocardiogram (1) that of the detailed analysis of the individual complexes or waves which will be largely covered in the present chapter and (2) that of the presentation of the characteristics of the records as a whole that is of the patterns which will be presented largely in other chapters for

example the electrocardiographic patterns of certain congenital defects of mitral stenosis of the hypertensive heart and the cor pulmonale of pericarditis and of myocardial infarction

ELECTROCARDIOGRAPHIC LEADS

The first and fundamental step in studying electrocardiograms is to become familiar with the so called electrocardiographic leads An electrocardio graphic lead is the connection of any two parts of the body by electrodes and wires with the recording galvanometer Although two electrodes may be at tached to any parts of the body (if they are not both too far from the heart or too close together) to lead the heart current to the galvanometer it has become customary for convenience and other reasons to make use clinically of the forearms the left leg and the precordium An esophageal lead point to explore the left atrium and base and posterior portion of the left ventricle has been proposed and tried with results of some interest but the procedure is not clinically practicable

Direct leads from various points on the heart surface itself present the most detailed information possible concerning the spread of the excitation wave and aberrations thereof to the individual heart chambers and their anterior posterior and lateral walls The best substitute for such direct leads in man has been found to be precordial leads with exploring electrode placed on the skin as directly as possible over the part of the heart which it is desired to study Thus many thoracic lead points are possible in the various intercostal spaces and around the chest and even in the esophagus We have not yet nearly enough information to be sure of the most desirable positions and indeed they are already known to vary from person to person according to the body build and the position and type of heart disease but certain points have already been selected and made the object of considerable study in normal and abnormal subjects more about these below An important con sideration in obtaining these precordial or close up leads is that the other or as it is sometimes called indifferent remote or peripheral electrode should be placed far from the heart itself on one of the extremities or on the back or by an ingenious arrangement introduced by Wilson to neutralize the effect of any one extremity by connecting all four extremities to a central terminal as the remote electrode point The concentration of interest on the precordial leads initiated what has been called essentially a unipolar lead

Quickly following suit unipolar limb leads have been introduced to join the unipolar and bipolar chest leads they were at first in major part elaborated by Goldberger (1947) In the early days of these so-called unipolar limb leads it was thought that they had a rather mysterious superiority over the old classical bipolar limb leads particularly in revealing more accurately the electrical (and also often the anatomic) position of the heart and otherwise obscure myocardial disease but more recently it has been shown by Gr and others that they actually merely supplement the bipolar limb

allow us to establish with greater accuracy the projection of the axis and abnormalities thereof on the frontal plane of the thorax thus expanding Einthoven s triangle (see below) into a figure with six axes the three of the unipolar leads being perpendicular to the three of the bipolar leads so that there is only a 60 degree instead of a 120 degree interval between the axes (as will be illustrated later in the chapter)

Although the very first published electrocardiogram (Waller 1887) was a chest lead convenience and chance led early electrocardiographers away from the thorax itself to limb connections and only in late years has there been a return to the precordium as an important focus of attention The precordial leads at this writing (1950) appear to have a double value as compared with the limb leads they reveal the electrical axis projection on the anteroposterior (more or less sagittal) plane at right angles to the frontal plane thus completing the resultant projection of the direction and magnitude of the electrical axis in space but also because of their close proximity to the heart itself they show more clearly myocardial abnormalities closest to th m Nevertheless it is not likely that the limb leads as now taken will be abandoned soon inasmuch as they readily reveal normal variations and abnormalities in the frontal plane The heart is a solid body and so should be explored electrically from all directions Eventually technics such as those developed by Duchosal and by Goldman (see below) or something newer still may replace the present procedures but as yet they have not been developed for practical routine use

In summary the reasons for taking these three types of leads are as follows We continue to register the *bipolar limb leads* because we are familiar with them after many years of use, because they clearly suffice to demonstrate the mechanisms responsible for tachycardia bradycardia and arrhythmia because they are important in helping to establish the projection of the electrical axis and abnormalities thereof in the frontal plane and because they have become in many instances a part of the useful electrocardiographic patterns with which we have become familiar during the past decade such as those of the acute cor pulmonale congenital atrial septal defect and advanced mitral stenosis (or chronic constrictive pericarditis involving preponderantly the left heart chambers) The *unipolar limb leads* are registered because they are especially helpful in demonstrating the position of the heart with or without complications of heart disease itself thus the right arm lead always (except in cases with dextrocardia) faces the interior of the heart and so normally all its complexes are inverted the left arm faces the outside wall of the heart when the heart lies horizontally or diagonally with resultant upright complexes and the inside of the heart (as does the *right arm lead) when the heart is vertical giving inverted QRS and T* waves the left leg lead never faces the inside of the heart although it is at right angles to its axis when it lies horizontally thus yielding under such conditions small almost isoelectric complexes The *unipolar precordial leads* are registered because of their double value just discussed in the preceding paragraph

Thus ordinarily now the three bipolar and the three unipolar limb leads

and several (preferably six) precordial leads are registered for each patient studied these leads have been called Leads 1 2 3 aVR aVL aVF and Precordial or Chest Leads 1 to 6 or more respectively (Figure 41) In routine interpretation at the present time (1951) it is convenient to analyze first the precordial leads since they often give the most information

BIPOLAR (CLASSICAL) LIMB LEADS

Lead 1 consists of the connection of the right lower arm to one end of the galvanometer string and of the left lower arm to the other end so that the preponderant spread of the action current (which has been called the wave

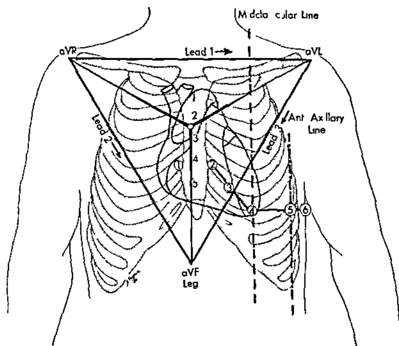


FIG 41 Diagram showing bipolar limb leads (1 2 3) unipolar limb leads (aVR aVL, aVF) and precordial leads (V to V inclusive) The outline of the heart is shown under the sternum and ribs the level of the first five interspaces is indicated Einthoven s triangle is represented as is also the spatial relationship of the remote electrode to the limb electrodes in the case of the unipolar limb leads

of relative negativity) in the direction of the lead that is from right arm to left is represented normally in the electrocardiogram by an upright deflection of the string shadow while its reverse direction is represented by an inverted deflection

Lead 2 consists of a similar arrangement but with electrodes on right arm and left leg Either leg may be used with little or no change in the records obtained since both legs show almost the same difference of electric potential

allow us to establish with greater accuracy the projection of the axis and abnormalities thereof on the frontal plane of the thorax thus expanding Einthoven s triangle (see below) into a figure with six axes the three of the unipolar leads being perpendicular to the three of the bipolar leads so that there is only a 60 degree instead of a 120 degree interval between the axes (as will be illustrated later in the chapter)

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Thus ordinarily now the three bipolar and the three unipolar limb leads

possible over the cardiac apex However it rather quickly became apparent that even with care it was not always possible so to place it that even though it were so placed it would usually emphasize normality or abnormalities of but a localized area of the heart wall and that it might be so close to the ventricular sulcus or so perpendicular to the spatial axis of the heart that a slight displacement to either side would shift its position from one ventricle to the other or from negative to positive side of the anteroposterior plane of the thorax (or vice versa) with a great change in the pattern Therefore an isolated *Lead 4* was given up by most workers in the field a few years ago

It was also stated in the last edition of this book that multiple precordial (chest) leads should be taken in special or doubtful cases and that the author and his colleagues were taking three such leads (CF CF_4 and CF_5) when necessary rarely more at that time Our own experience and that of many others soon caused us to take three precordial leads routinely with the exploring electrode at points 2 4 and 5 and as time went on over 2 4 and 6 instead and with Wilson s central terminal (V) for the indifferent lead point instead of the left leg (as had been our choice) or the right arm (as was often the choice of others) Finally with more experience in the course of time we began to take all six precordial V leads in addition to the six limb leads mentioned above so that for the sake of the valuable extra information afforded we now take 12 routine leads instead of the 3 that we took at the time of the first edition of this book (1931) the 4 that we frequently took at the time of the second edition of the book (1937) and the 6 that was our custom at the time of the third edition of the book (1944) In fact on occasion we may now explore further still as in the case of a special atrial lead (high up over the right atrium) or of a lead (sometimes called 7) on the back at the left posterior axillary line It is still too early to know how far we had best explore and just what technics we shall eventually use

Multiple precordial leads (Figure 41) have become standardized as follows the prefix depending on the position of the indifferent electrode or lead point— CR (chest—right arm) CL (chest—left arm) CF (chest—left leg) and CV usually abbreviated now to V

1 or CR_1 CL_1 CF_1 CV_1 or V_1—the exploring electrode at the *right* border of the sternum in the fourth intercostal space

2 or CR CL CF CV or V—the exploring electrode at the *left* border of the sternum in the fourth intercostal space

3 or CR_3 CL_3 CF_3 CV_3 or V_3—the exploring electrode midway on the line joining 2 and 4

4 or CR_4 CL_4 CF_4 CV_4 or V_4—the exploring electrode at the left midclavicular line in the fifth intercostal space We used to try to place this electrode at the cardiac apex but the variability of the position of the latter both in health and in disease rendered that location very unreliable and unsatisfactory

5 or CR CL CF CV or V—the exploring electrode at the anterior

during the cardiac cycle the left leg is however the customary lower point

Lead 3 consists of the connection of the galvanometer with left arm left leg in comparison with Lead 2 the left leg lead continues to be the contact while the left arm is substituted for the right arm

Thus these three lead points right arm left arm and left leg when connected form a triangle which is essentially equilateral Electrically and metrically Lead 2 is equal to the sum of Leads 1 and 3 since the difference of electric potential between right arm and left leg is the same whether connect the lead points directly or in a roundabout way Therefore the P_2 should equal P_1 plus P QRS should equal QRS_1 plus QRS_3 and T should equal T_1 plus T_3 (these letters refer to atrial and ventricular deflections in the electrocardiogram soon to be discussed while the appended numbers refer the particular leads—1 2 and 3) Similarly Lead 2 minus Lead 1 equals Lead 3 and Lead 2 minus Lead 3 equals Lead 1 This fact although useful clinically in checking the accuracy of standardization of the various leads is often ignored

UNIPOLAR LIMB LEADS

Lead aVR is the new customary so called augmented (a) that is amplified 50 per cent unipolar (V a symbol) right arm (R) lead The exploring electrode is attached to the right arm and connected to one pole of the galvanometer while the other pole is connected to the indifferent lead point which in the case of the unipolar limb leads has been found to serve best when attached to the three limbs not being explored V is a designation introduced by Johnston—personal communication 1951—to indicate leads taken with a central terminal and derived from its usage by electrical engineers and physicists as a symbol of electrical potential it was not originally intended as an abbreviation for vector

Lead aVL is the augmented unipolar left arm lead with exploring electrode on the left arm and indifferent lead point connected to the right arm and both legs

Lead aVF is the augmented unipolar left leg (F for foot) lead with exploring electrode on the left leg and indifferent lead point connected to both arms and right leg

It is important and convenient to know that when added together the three unipolar limb leads aVR aVL and aVF equal zero

PRECORDIAL (CHEST OR THORACIC) LEADS

In the last (third) edition of this book much was said about *Lead 4* which had been called the standard or indeed even the classical" chest lead It had been taken by attempting to place the exploring electrode as near as

ighth and ninth leads over the left back and right anterior chest leads numbered from midline to the right like the precordial leads and as advised by Kisch with the first lead point at the midsternum (level of fourth interspace) for both sides

It is obvious that the unipolar chest leads taken as Wilson has recommended (CV) leads give a more accurate appraisal of the potential at the various precordial lead points than do the bipolar leads although there is by no means so great a difference as in the case of the unipolar and bipolar

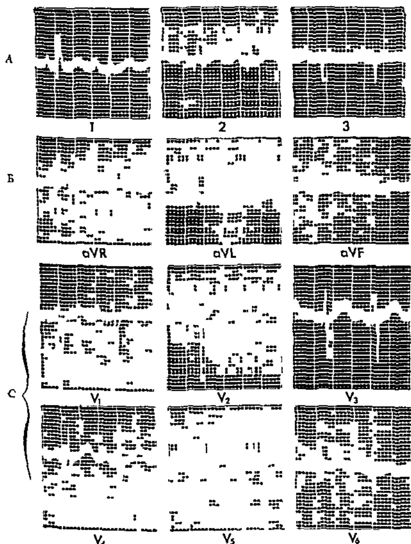


FIG 43 Electrocardiogram of normal individual of heavy build with horizontal heart position (*A*) Bipolar limb leads 1 2 and 3 (*B*) unipolar limb leads aVR, aVL, and aVF (*C*) six precordial leads V to V inclusive Time = 0 04 and 0 20 second amplitude 1 mm = 0 10 mv

limb leads This is of course due to the fact that the greater the diff in distance of two electrodes from the heart the less the error due ... potential of the point to which the indifferent electrode is attached Thus th bipolar chest leads described above approach in accuracy the unipolar chest leads of Wilson For this reason and especially for the sake of universa uniformity it is suggested that for routine use the V leads be now employed a has been my own recent custom



FIG 44 Electr... liogram of normal tall individual with vertical heart posit... (A) Bipolar limb ... 1 2 and 3 (B) unipolar limb leads aVR aVL and a... (C) six precordi... V to V inclusive Time = 0 04 and 0 20 second ampli... mm = 0 10 mv

Intracardiac and esophageal leads have been used in research and for study of very special cases the former during catheterization of the right atrium and right ventricle and the latter for exploration of the left atrium and posterior wall of the left ventricle They serve as unipolar leads to explore these particular parts of the heart and although during acute myocardial infarction it is not wise to subject the patient to esophageal electrocardiography it is possible in chronic cases to identify a posterior myocardial scar and also to uncover atrial action not apparent in other leads The right intra atrial electrocardiogram shows normally an inverted *P* wave high in the atrium in the vicinity of the s a node an upright *P* wave low in the atrium and a diphasic *P* wave in intermediate positions while the ventricular complex varies from a *QS* to a *QR* most commonly or even less often (near the ventricle) to a *RS* all with negative *T* waves The right intraventricular electrocardiogram shows normally an upright *P* wave and an *RS* with a negative *T* Esophageal leads show a slightly later *P* wave over the left atrium by about 0 05 second than the *P* wave recorded by the right intra atrial electrode

In the esophageal lead the *P* wave is as a rule unusually prominent and high and the *QRS* and *T* waves are normally inverted unless the polarity is reversed in which case an inverted *T* wave is indicative of disease (usually infarction) of the posterior wall of the left ventricle

CARDIAC VECTOR AND ELECTRIC AXIS

A vector is a force which has direction and magnitude and electrically either a negative or a positive charge In electrocardiography it has been loosely called the electrical axis of the heart Fundamentally electrocardiography is the analysis of the cardiac electrical vectors and there are various technics for their demonstration all of which are more or less crude and in the process of further development including the old classical bipolar limb leads with the much debated but still scientifically applicable Einthoven triangle the unipolar limb leads the precordial leads and the more basic but least developed technic of all namely that of vectorcardiography

When the excitation wave spreads from normal or abnormal pacemaker through the heart it is attended by a wave of electric activity which takes a complicated manifold path (see Figure 39 page 183) The diffuse course can be represented by the *QRS* loop a curve not lying in a single plane but in space as does the heart itself A further reduction of this curve has hitherto been necessary to suit the limited boundaries of electrocardiography and so we can determine its projection on the anterior plane of the body to fit into the triangle of the three classical leads or on any other plane for example specifically sagittal or horizontal Finally for further convenience the curve is simplified by constructing its resultant a straight line to show the consequent angle and magnitude This resultant of the projection of the true axis of the distributed electric potential of the heartbeat is what we briefly designate as the electric axis of the electrocardiogram It can be determined by calculation

from any two of the three classical limb leads by formula or by diagram usi what is called Einthoven s triangle It has been of some clinical interest a value to make this calculation in cases showing an abnormal deviation of t angle (the normal range of angle is from −20 to +100 but usually +? to +70°) The formula is as follows *tangent of alpha* $= \frac{2e - e_1}{e_1\sqrt{3}}$ whi alpha equals the angle between the axis and the horizontal *e* the amplitu in millimeters of the *QRS* wave in Lead 2 and e_1 that of the *QRS* in Lead The length of the axis or the manifest potential difference (E) is calculat from the following formula $E = \frac{e}{\cos(\alpha - 60)}$ More convenient than th formulas has been the employment of the diagram of the triangle of t leads (Figure 45 Einthoven s triangle) Leads 1 and 3 are usually employ in this calculation The amplitude of $R_1 - S_1$ is plotted on the Lead 1 li and that of $R_3 - S_3$ on the Lead 3 line perpendiculars are dropped from th points to their points of intersection Lines are then drawn out from the cen of the circle through these points of intersection to the circumference of t circle the angles with the horizontal diameter of the circle the zero line a read off the degrees being noted as positive around the semicircle clockw to 180 and as negative counterclockwise This is a crude but clinically co venient and useful method It affords only a very general measurement a shows no detail of the axis deviation If at the present time however grea detail and accuracy are attempted the method becomes complicated and dil cult Although it is of some academic interest to know not only the results axis deviation but its whole curve that is the individual deviations at vario phases it is of much greater interest to know the direction of the curve space for example how much of it is bent backward in the anteroposteri plane a feature not shown at all in the frontal plane It is to be noted that secure adequate information accurately for even one (e g the frontal) pla two electrocardiographic leads must be registered simultaneously to make su of the synchronicity of phases for example the top of the *QRS* peak in Lead is often not synchronous with either peak (or nadir) of downstroke in Lead A further development of the representation and analysis of the cardiac vect (electric axis) in space has been the construction of the vectorcardiogra both by projection on the three planes and by tridimensional models (se below)

The direction of the resultant electric axis of the heart in the frontal plai lies within wider limits than does the anatomic axis both normally and al normally The normal electric axis lies between the degrees −20 and +10 of Einthoven s triangle (Figure 45) If the angle is more minus than −20 that is much above the horizontal there is so-called abnormal *left axis* devia tion and if it is beyond +100° that is considerably to the right of th vertical there is abnormal right axis deviation

The term abnormal left and right axis deviation as applied to the classic bipolar limb leads does not have the same significance as left and ri

ventricular preponderance Displacement of the heart upward by a high diaphragm so that the heart lies horizontally will give abnormal left axis deviation even though the left ventricle remains normal while a low diaphragm with vertical heart position will tend to give abnormal right axis deviation even though the right ventricle is small and the left ventricle actually preponderant It is true however that when we find high degrees of abnormal

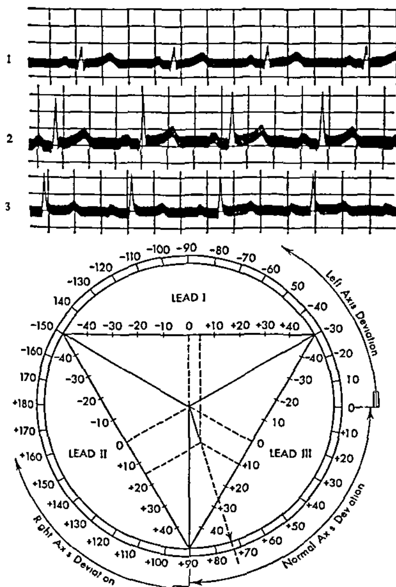


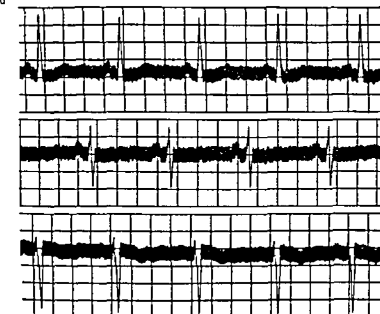
FIG. 45 Electrocardiogram (Leads 1, 2 and 3) and Einthoven's triangle showing normal angle of the electrical axis

from any two of the three classical limb leads by formula or by diagram using what is called Einthoven s triangle It has been of some clinical interest and value to make this calculation in cases showing an abnormal deviation of the angle (the normal range of angle is from −20° to +100 but usually +30 to +70°) The formula is as follows *tangent of alpha* $= \frac{2e - e_1}{e_1\sqrt{3}}$ where alpha equals the angle between the axis and the horizontal e the amplitude in millimeters of the *QRS* wave in Lead 2 and e_1 that of the *QRS* in Lead 1 The length of the axis or the manifest potential difference (E) is calculated from the following formula $E = \frac{e}{\cos(a - 60)}$ More convenient than these formulas has been the employment of the diagram of the triangle of the leads (Figure 45 Einthoven s triangle) Leads 1 and 3 are usually employed in this calculation The amplitude of $R_1 - S_1$ is plotted on the Lead 1 line and that of $R_3 - S_3$ on the Lead 3 line perpendiculars are dropped from the points to their points of intersection Lines are then drawn out from the center of the circle through these points of intersection to the circumference of the circle the angles with the horizontal diameter of the circle the zero line are read off the degrees being noted as positive around the semicircle clockwise to 180 and as negative counterclockwise This is a crude but clinically convenient and useful method It affords only a very general measurement and shows no detail of the axis deviation If at the present time however greater detail and accuracy are attempted the method becomes complicated and difficult Although it is of some academic interest to know not only the resultant axis deviation but its whole curve that is the individual deviations at various phases it is of much greater interest to know the direction of the curve in space for example how much of it is bent backward in the anteroposterior plane a feature not shown at all in the frontal plane It is to be noted that to secure adequate information accurately for even one (e g the frontal) plane two electrocardiographic leads must be registered simultaneously to make sure of the synchronicity of phases for example the top of the *QRS* peak in Lead 1 is often not synchronous with either peak (or nadir) of downstroke in Lead 3 A further development of the representation and analysis of the cardiac vector (electric axis) in space has been the construction of the vectorcardiogram both by projection on the three planes and by tridimensional models (see below)

The direction of the resultant electric axis of the heart in the frontal plane lies within wider limits than does the anatomic axis both normally and abnormally The normal electric axis lies between the degrees −20 and +100 of Einthoven s triangle (Figure 45) If the angle is more minus than −20° that is much above the horizontal there is so-called abnormal left axis deviation and if it is beyond +100° that is considerably to the right of the vertical there is abnormal right axis deviation

The term abnormal left and right axis deviation as applied to the classical bipolar limb leads does not have the same significance as left and right

Lead



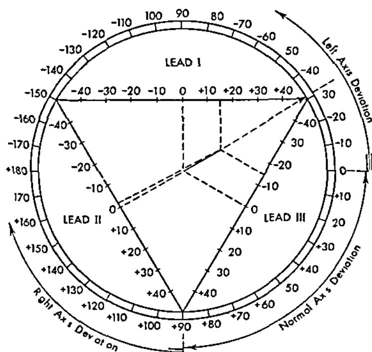


FIG 46 Electrocardiogram and Einthoven's triangle showing left axis deviation

average normal angle to an abnormal one (Figure 4 page 33) This influence of displacement may even give abnormal left axis deviation of great degree although it often but exaggerates the effect of other factors An interesting variation of this type consists of complete negativity of Lead 3 all the complexes—*P* *QRS* and *T*—being inverted this phenomenon is often found in short fat individuals with high diaphragms

2 Preponderant enlargement of the left ventricle is a common cause or accompaniment of left axis deviation of high degree Chronic hypertension and chronic aortic regurgitation or stenosis are the most important of the known clinical conditions behind it (see Figure 97 page 477 and Chapter 26)

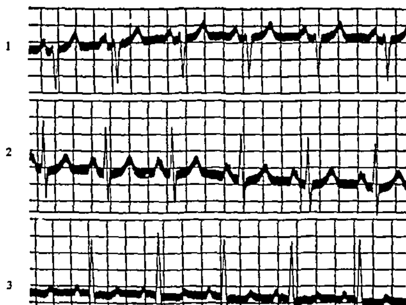
3 Left bundle branch block (see Chapter 34) The electrocardiogram of marked left bundle branch block has abnormally wide *QRS* waves over 0 1 second in duration with moderate amplitude above the baseline in Lead 1 and below the baseline in Lead 3, with rather low voltage or diphasic *QRS* waves in Lead 2 (see Figure 165 page 947) and broad notched downwardly directed *QRS* waves over the right ventricle and bifid or slurred *R* waves over the left in the multiple precordial leads Until fifteen years ago this type of electrocardiogram was thought to indicate right bundle branch block but convincing evidence from the precordial leads (with late arrival of th intrinsic deflection over the left ventricle) exposed the error of the earlier interpretation

4 Right ventricular premature beats (see Chapter 32) Isolated instances of abnormal axis deviation occur in the form of ventricular premature beats arising in the right ventricle or near the cardiac base The *QRS* waves are deformed much as in left bundle branch block but their amplitude is usually much greater In a well marked instance of right ventricular premature beat the QRS_1 is relatively high the QRS_3 is deep the *QRS* is diphasic and often of low voltage and the precordial *QRS* shows an early intrinsic deflection over the right ventricle Years ago these extrasystoles were thought to arise in the left ventricle

Abnormal right axis deviation (Figure 47) much less common than abnormal left axis deviation results from five factors

1 A vertical heart position or rotation of the heart on its other axes may give rise to abnormal right axis deviation usually not of great degree the angle rarely measuring more than +95° in the normal person but sufficient to mask other conditions It is by far the commonest cause of right axis deviation Deep inspiration may give temporarily a slightly abnormal right axis deviation when the electrocardiogram in quiet breathing shows a tendency toward it Displacement of the heart to one side or the other by fluid or by air in the pleura or by lung retraction or pleural adhesions affects the position of the heart as a rule in toto along with the mediastinum withou causing any important change in axis deviation as does also shifting of position from one lateral recumbency to the other as noted above

2 Preponderant enlargement of the right ventricle with its attendant shift in position of the heart particularly by clockwise rotation is the commonest



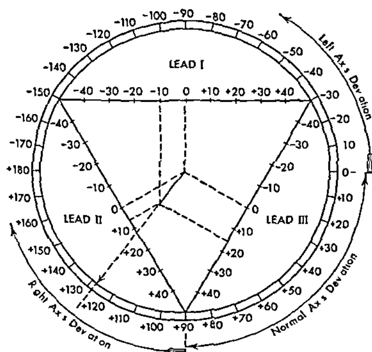


FIG 47 Electrocardiogram and Einthoven's triangle showing abnormal right axis deviation in a case of mitral stenosis of high degree

cause of markedly abnormal right axis deviation in which there is a sharp moderately deep S_1 with little or no R_1 a diphasic *QRS* of little voltage a high R_3 with little or no S_3 and relatively high R waves over the right ventricle and prominent *S* waves over the left ventricle in the precordial leads During the first few weeks of life right axis deviation is often present normally in slight degree After that age moderate or high degrees of right axis deviation are caused by three clinical conditions mitral stenosis congenital defects and pulmonary disease Mitral stenosis is frequently found without abnormal right axis deviation but when that electrocardiographic sign is present especially if there is atrial fibrillation and no obvious sign of congenital heart disease that valve lesion is usually found to be present (Figure 129 page 680) Congenital pulmonic stenosis and interatrial septal defects are rarely if ever found without abnormal right axis deviation by electrocardiogram they cause a higher degree of it than does any other condition (see Figure 73 page 320) Rarely the cause of abnormal right axis deviation is chronic pulmonary disease in particular silicosis or other cause of extensive fibrosis Very rarely pulmonary endarteritis may be a factor

3 Right bundle branch block is shown electrocardiographically by abnormally wide *QRS* complexes directed downward in Lead 1 and upward in Lead 3 or by wide S_1 waves (see Figure 166 page 948) In Lead 2 the *QRS* wave is diphasic as a rule and of low voltage and in the multiple precordial leads it is M shaped over the right side of the heart and shows a prominent *R* wave and wide *S* wave over the left This was formerly called left bundle branch block (see Chapter 34)

4 Left ventricular premature beats are isolated instances of abnormal right axis deviation giving high wide *QPS* complexes in Leads 2 and 3 *QRS* waves often of low voltage slightly or moderately inverted in Lead 1 and with wide *QRS* waves in the precordial leads with earlier intrinsic deflections over the left ventricle A premature beat arising from the left ventricle although near the right ventricle has been shown experimentally to give rise to a *QRS* complex of left ventricular premature beat type But ventricular premature beats are often neither of definitely right nor of definitely left ventricular type in the electrocardiogram in such cases they may arise in the septum or junctional tissue

5 Congenital dextrocardia shows a typical electrocardiogram in about half the cases that is where there is transposition with general situs inversus (see Figure 65 page 303) There is a complete inversion of all complexes of Lead 1 and an interchange of the usual Leads 2 and 3 due to the fact that with relation to the heart in such a case the right arm corresponds to the left arm of the person with the heart in normal position and the left arm to the right When an electrocardiogram shows a completely inverted Lead 1 it is pathognomonic of congenital dextrocardia provided there is no error in technic namely a crossing of electrode wires The precordial leads show the usual normal characteristics when the exploring electrode is placed over the right side of the chest

Vectorcardiography A further and natural evolution of the study of the cardiac vector is its determination and demonstration in space that is in three dimensions and also in time which is of prime importance too since the duration as well as the distance direction and magnitude of the cardiac vector is significant Various technics have been introduced to study the vector projected on the frontal plane as already noted including among others that re cently devised by Goldman using the cathode ray oscillograph and many lead points over the entire precordium which result in waves of darkness and light representing *P* *QRS* and *T* waves sweeping over the field

Also desirable as an eventual goal when it can be routinely introduced is the spatial (and time) recording of the cardiac vector which has been called vectorcardiography Various investigators have studied the problem Mann was one of the first who did so calling the resulting curve the monocardiogram (1920 and 1938) Duchosal and Sulzer (1949) are also pioneer workers who have developed the method more fully with the actual construction of models of the *P* *QRS* and *T* waves (vectorcar diography) based on the projections of cathode ray oscillograms of the cardiac vector on two planes of a trihedron with the time marked off by beads attached to the wire loops representing the course of the vectors (Figure 48) Figure 49 shows the relationship of the trihedron of Duchosal and Sulzer to Ein thoven s triangle and the unipolar chest lead points Much time will be needed to determine the range of normal vectorcardiograms and abnormal patterns

My friend and former associate Dr J W Hurst of Atlanta Georgia ex perienced in recent developments in certain technics of the application of vectorcardiography in this country has kindly prepared for me the following insert (personal communication March 1951)

Grant and his co workers have presented a method for determining the spatial direction of the fundamental electrical forces of the heart by simple inspection of routine electrocardiographic leads Since this method appears promising it is mentioned here for completeness For greater details and proof of the method the reader is referred to the Bibliography

To d termine the direction of the mean *QRS* *ST* and *T* forces in the frontal plane the six extremity leads are inspected to determine which lead has the largest deflection and which lead has the sm illest deflection The resultant area of each deflection is used to determine its relative size The resultant area is determined by adding the positive portions of the curve to the negative portions algebraically The mean vector will be parallel to the lead axis with the largest resultant deflection or perpendicular to the lead axis with the smallest resultant deflection and its direction must satisfy the polarity of all six extremity leads With practice one will soon learn to interpolate between the extremes of vector positions just mentioned so that the range of error will be only 5 to 10 degrees The direction of the instantaneous vectors can be determined in a similar manner by breaking up the *QRS* and *T* deflec tions into small individual portions If one remembers that Lead 1 + 3 = 2 and that aVR + aVL + aVF = 0 then the determination of the direction of

the various vectors becomes quite accurate By the above reasoning one can determine the frontal plane projection of the mean spatial *QRS ST* and *T* vectors and spatial *QRS ST* and *T* loops

After identifying the direction of the frontal plane projection of a spatial vector one then locates the transitional complex in the precordial leads (A transitional complex is equally negative and positive or resultantly zero) The transitional complex is recorded along the transitional pathway on the chest which is produced by a plane perpendicular to a spatial vector at its origin extended to the surface of the volume conductor The location of this plane which is perpendicular to the spatial vector under study will therefore deter

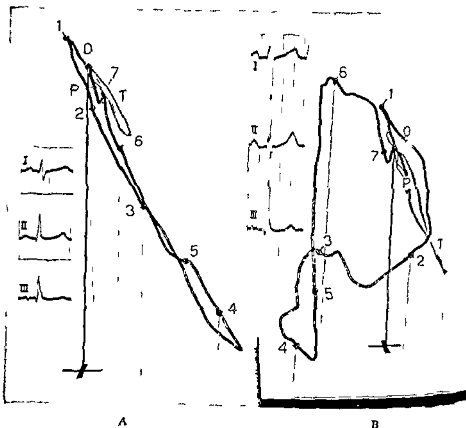


FIG 48 (*A*) Photograph of wire loop representing the vectorcardiogram of a normal individual The timing of the long obliquely placed *QRS* loop indicated by heavy black wire is shown by beads from 0 to 7 (time interval = 0 01 second) The *P* loop is made of thin wire scarcely visible The *T* loop is grey in color The point of origin of all three loops *P QRS* and *T* is zero A black column supports the model At the bottom of the stand a cross represents the normal axes of the body the vertical bar the antero-posterior and the horizontal bar the transverse The electrocardiogram (limb leads I II and III) is shown at the left of the loop (*B*) Wire loop representing the vectorcardiogram of a case of the tetralogy of Fallot with the graphs of the complexes and the electrocardiogram represented as in the case of *A* (Kindness of Dr Pierre Duchosal Geneva Switzerland)

mine the anterior or posterior displacement of a vector from the frontal plane thus identifying its spatial position If the thorax is assumed to be a cylinder which is a reasonable assumption electrically speaking it is quite easy to visualize the transitional pathway and its relationship to the spatial vector The method described allows one to determine the mean spatial vectors and by similar reasoning the spatial instantaneous vectors can be visualized The range of error in determining the spatial direction of electrical forces approaches 15 degrees

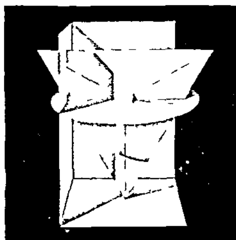


FIG 49 Drawing in perspective of the plans of derivations according to several systems The rectangular trihedron symbolizes the derivations of the vector the equilateral triangle that of the limbs and the ellipse those of the precordium (Kindness of Duchosal and Sulzer Figure 43 page 88 of their book *La Vectocardiographie* S Karger Bale and New York 1949)

In a general sort of way the *QRS* vector indicates the direction of the electrical field in the chest and it becomes totally unnecessary to memorize various deflection contours in order to determine such a position The spatial *QRS T* angle is an extremely useful tool It should be apparent that the *QRS* vector and *T* vector produce the sides of the parallelogram which is necessary to construct the ventricular gradient and therefore the *QRS T* angle incorporates certain of the properties of the gradient The spatial *QRS T* angle varies with age and in the normal adult is usually less than 60 degrees

The electrocardiogram of a patient with a normal heart is shown analyzed by the vectoral method in Figure 50

The electrocardiogram of a patient with an extensive anterior myocardial infarction is shown analyzed by the vectoral method in Figure 51

Electrocardiographic gradient Closely related to the cardiac vector and the electric axis is the so-called gradient which may be calculated for either atria or ventricles although to date attention has naturally been focused as in other such studies on the ventricles The ventricular gradient as defined by Burch

and Winsor (1949) is a vector expression (in quantitative terms) of the relative variations in duration of the excited state in the different portions of the ventricular musculature Thus g (the ventricular gradient as projected on the frontal plane of the body) = the sum of A_{QRS} (the mean manifest magnitude of the *QRS* complex determined algebraically and measured in microvolt seconds or units i e the mean force of the depolarization process of the ventricular musculature) plus A_T (the mean manifest magnitude of the *T* wave which represents the repolarization process in microvolt seconds or units) The caret placed over the symbols indicates a vector value

The technic of the measurement of the ventricular gradient consists of

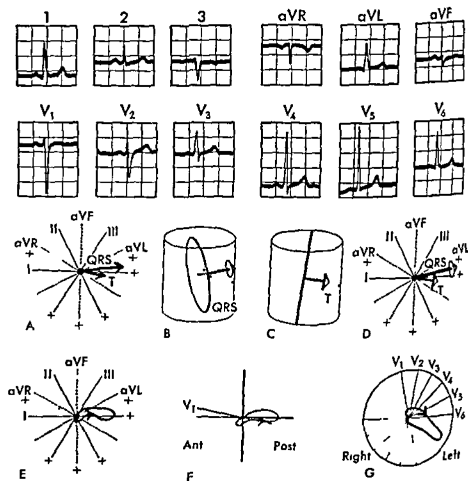


FIG 50 Thirty seven year-old normal male illustrating a horizontal position of the mean *QRS* vector (*A*) Mean *QRS* and *T* vectors as seen in the frontal plane (*B*) mean spatial *QRS* vector as seen in a cylindrical volume conductor (*C*) mean spatial *T* vector as seen in a cylindrical volume conductor (*D*) final "summary" figure to illustrate the spatial *QRS* and *T* electrical forces (*E*) frontal plane *QRS* loop (*F*) saggital plane *QRS* loop and (*G*) coronal plane *QRS* loop seen from below (Kindness of Dr J Willis Hurst Atlanta)

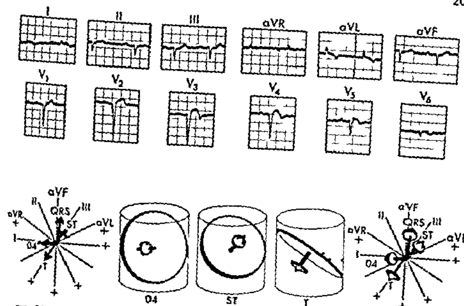


FIG 51 The electrocardiogram shown above is from a 50 year-old male with a char acteristic history of myocardial infarction The figure to the left shows a six axial lead arrangement which is produced by superimposing the unipolar extremity lead axes on the tri axial reference system of Bayley This figure shows the frontal plane projection of the spatial *QRS ST T* and 04 vectors Note that the mean *QRS* is only slightly positive in Lead 1 and is negative in Leads 2 and 3 and also fits the polarity of the unipolar extremity leads The mean *T* vector is perpendicular to Lead aVR and there fore is largest in Lead 3 The mean *ST* vector is slightly negative in Lead aVR and the first 04 second of the *QRS* loop is approximately perpendicular to Lead aVF The edge of the circular disc represents the transitional pathway along which transitional complexes will be recorded The 04 second vector is tilted markedly posteriorly since the initial deflection is negative in Leads V The *ST* vector is tilted markedly anteriorly since the *ST* segment is elevated in all the chest leads The *T* vector is tilted only slightly anteriorly since the *T* wave is positive in Lead V and negative in Leads V, , , , In general the 04 "dead zone vector is directed away from an area of myo cardial infarction and the *T* vector is directed away from the ischemic zone surrounding the area of infarction The *ST* vector is directed toward the area of myocardial injury surrounding the area of infarction The tracing above represents an extensive anterior myocardial infarction since the 04 vector is directed away from the anterior ventricular wall and the *ST* vector points toward the same area The *T* vector is directed away from the lateral wall of the left ventricle The diagram to the right illustrates how the spatial vectors are recorded routinely in clinical practice (Figure and legend through the kind ness of Dr J Willis Hurst Atlanta)

The 04 vector refers to the initial electrical force acting during the first 04 second of the *QRS* loop

measuring the sum of the areas (A) in microvolt (one millionth volt) seconds under the *QRS* and *T* waves above the baseline in any two leads (preferably Leads 1 and 3) and subtracting the sum of areas below the baseline (Figure 52A) In the case of a single normal muscle strip (Figure 52B) the gradient would be zero since the depolarization area (R) above the baseline would be neutralized by the repolarization area (T) below the baseline In human electrocardiography however the situation is very different there being many

heart muscle masses with varying individual influences per se and as affected by changes in position and rate of the heart as well as by disease Thus since in the frontal plane the routine limb leads show normally preponderant upright T waves as well as preponderantly upright QRS waves the normal ventricular gradient in man has been found to average +52 microvolt seconds or 13 0 units (1 unit = 4 microvolt seconds) the range is not certain but has been put at a maximum of 23 0 units and a minimum of about 2 5 units (Burch and Winsor 1949) The gradient of QRS (A_{QRS}) varies from about +12 0 to about −3 5 units There is as yet little clinical applicability of the ventricular gradient although primary changes in A_T (i e not dependent on variations of the QRS wave) may be distinguished by this method

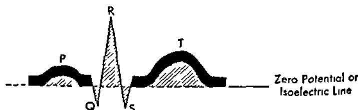


FIG 52A Diagram showing the areas subtended by the P and QRS complexes and the area under the T wave Areas above the isoelectric line are considered to be positive values and those below the isoelectric line are negative

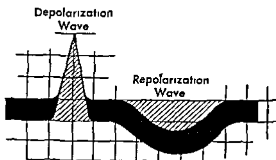


FIG 52B The process of depolarization and repolarization results in two separate waves which include areas of equal size (*A Primer of Electrocardiography* 2nd ed 1949 [1st ed 1945] Kindness of Drs George Burch and Travis Winsor and Lea & Febiger Philadelphia)

ELECTROCARDIOGRAPHIC COMPLEXES AND TIME INTERVALS

THE ATRIAL DEFLECTION OR P WAVE

The normal P wave Electrical activity of the atria is as a rule better defined and studied in Lead 2 than in the other routine leads because the axis of the P (atrial) wave is commonly parallel to Lead 2 for special analysis in difficult cases however the first precordial lead V_1 may be useful or, best of all a lead with electrode in the third interspace just to the right

of the sternum Analysis of the normally inverted *P* wave in Lead aVR may also prove helpful

The P wave of Lead 2 of the electrocardiogram is normally a blunt rounded sometimes slightly notched or scalloped upright deflection 1 to 3 mm high (each millimeter represents in a properly standardized record one tenth of a millivolt) and not over 0 1 second wide at the lower border of the baseline between corresponding points of upstroke and downstroke This wave represents the spread of excitation over the atria along the muscle bundles from the normal starting point the pacemaker at the head of the sinoatrial node which lies at the junction of the superior vena cava and the right atrium (Figure 39 page 183) The atrial electric axis which is the resultant of the spread of current in all directions over the muscle of right and left atria is normally directed down and to the left in its projection on the anterior plane of the body which is that represented by the routine electrocardiogram The *P* wave itself is very short in time interval and represents only about one third of the duration of atrial systole it is followed however by a slight change in baseline of varying extent usually directed downward coinciding in time with the rest of the atrial systolic interval but as a rule concealed by the superimposition of the first ventricular complex or *QRS* wave In heart block this late evidence of atrial electric activity may sometimes be clearly seen It has been called the atrial *T* wave or *Ta* deflection (Figure 53)

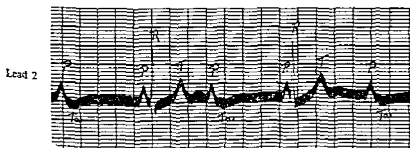


FIG 53 Electrocardiogram showing *Ta* waves in complete heart block Lead 2

The P wave of Leads 1 and 3 In Lead 1 the *P* wave is called P_1 It is of lower amplitude normally than in Lead 2 sometimes it is flat or isoelectric and so may be invisible rarely it may be greater than the *P* wave in Lead 2 (*P*) normally when the *P* wave of Lead 3 (P_3) happens to be inverted Very rarely the P wave may be inverted in Lead 1 when there is normal rhythm such a finding means congenital dextrocardia if an error has not been made in the attachment of the electrodes with resulting totally upside down Lead 1 When P_1 is 2 mm or more in amplitude it is abnormal and the same factors responsible for an abnormally high or wide *P* are also responsible for too large a P_1 In other respects too the discussion about P applies to P_1

In Lead 3 the P wave may normally be upright isoelectric diphasic or even slightly inverted It is therefore the least desirable of the three bipol limb leads for study of the atrial complex However arrhythmias may l present in this lead and not in the others and one may also wish to note the character of the P_3 wave to aid in the interpretation of atrial abnormalities in the other leads and of the significance of inversion of T_3

In the *unipolar limb leads* the P wave like the *QRS* and T waves varies normally in direction and amplitude with the position of the heart In the right arm lead (aVR) it is almost invariably inverted and often closely re sembles except for its direction the P wave of Lead 2 In the left arm and left leg leads it is upright and of variable height higher in aVL than in aVF if the heart lies horizontally and vice versa if the heart is vertical

In the *unipolar precordial leads* V_1 to V_6 inclusive, the P wave is not usually so well marked as in the limb leads it may be of fair amplitude however and more often upright than otherwise in the first position just to the right *of the sternum and when the right arm is used as the indifferent or distal lead* point in general it may be upright, isoelectric diphasic or inverted

Abnormalities of the P wave The description of the P wave abnormalities herein refers in particular to Lead 2 which as a rule of the routine leads shows them best

The P wave may show abnormalities of size and shape whether the heart rhythm is regular or not Moreover the P wave itself may remain normal in some instances of irregular or disturbed rhythm as in heart block Disorders of rhythm will be considered in the last three chapters of the book Sinus arrhythmia however demands a brief discussion now

Due to a variable activity of the pacemaker in the sinoatrial node caused by vagal influence and often associated with some bradycardia sinus arrhythmia (Figure 161 page 927) is generally a simple waxing and waning of rate with the intervals between normal P waves first decreasing and then increasing in phases related to the corresponding phases of respiration inspiration and expiration It is a normal phenomenon most common in children If very marked or not related to respiration it is an abnormal phenomenon in which case digitalization or faulty coronary circulation or an unknown factor may be responsible The P waves may decrease in amplitude with the periods of bradycardia as the pacemaker descends along the sinoatrial node usually they do not so decrease

Increase in amplitude (height) of the P wave is usually associated with increase in its width or duration although one may be present without the other An amplitude of 3 mm or more and a duration measured between corresponding points of upstroke and downstroke at the baseline of over 0 1 second are greater than the normal measurements in the subject at rest Although exercise and sometimes increased sympathetic tone with tachycardia induced otherwise than by exercise tend to increase the height of the P wave even above the usual normal limit a constant increase in height or width or both of the P wave is most often found in three conditions namely mitral

tenosis and two congenital anomalies atrial septal defects and the tetralogy f Fallot both of which especially the first are associated with considerable trial enlargement Hypertension especially with myocardial failure and less ommonly other ill defined conditions may cause high *P* waves in the electro ardiogram When this atrial deflection is abnormally high or wide it tends ilso to be abnormally notched sometimes the notching is so deep that the leflection appears doubled Increased width of the *P* wave with or without ncrease in height is more likely to indicate enlargement of the left atrium as n mitral stenosis while preponderant increase in height with or without in rease in width is more often found with enlargement of the right atrium as n the case of a congenital atrial septal defect

Decrease in amplitude may occur in vagal depression of the sinoatrial node with probable displacement of the pacemaker from the head of the node down toward the tail and this may be halfway or more along the sulcus terminalis toward the inferior vena cava This change in *P* wave may be seen to occur gradually or suddenly or it may be a constant finding it is frequently asso ciated with a slowing of the heart rate It may sometimes be produced through vagal stimulation by pressure over the carotid sinus but it also may occur indirectly through the effect of digitalis or it may infrequently occur spon taneously as for example during the slowing of the heart rate at the end of expiration The clinical condition in which an abnormally low in fact often almost isoelectric or flat *P* wave is regularly found is hypothyroidism (Figure 92 page 454) due to either myxedema or cretinism This smallness of the *P* wave in such cases accompanies a tendency to low voltage throughout the electrocardiogram particularly involving the *T* wave When the clinical con dition improves and the basal metabolic rate rises toward normal under treat ment with thyroid gland the *P* wave also becomes more normal Under other varied circumstances the *P* wave is occasionally found very low the reasons for which are not clear Heart failure alone does not cause the change

Absence of the P wave as a separate definite deflection results from several causes (1) In the first place this is most commonly due to atrial fibrillation in which orderly sequence of atrial contraction is replaced by irregular rapid incoordinated atrial movement (see Chapter 33) (2) In the second place the *P* wave may be replaced by regular instead of irregular baseline oscilla tions due to another condition closely related to atrial fibrillation namely atrial flutter (see Chapter 33) (3) In the third place the *P* wave may be partly or wholly buried in the *QRS* wave or in the *T* wave in cases of atrio ventricular block (Figures 53 and 164 page 935) of paroxysmal tachycardia (Figures 156 and 157 pages 879 881) and of premature beats whether of atrial or ventricular origin (Figures 154 and 155 pages 868 869) of reciprocal rhythm or ventricular escape (Figure 161 page 927) and finally of the rare atrioventricular nodal rhythm (Figure 163 page 932) In most instances of these abnormal rhythms the *P* wave does not exactly coincide either with the *QRS* wave or with the *T* wave and so it can be distinguished A mechanical tracing of the jugular pulse may in some of the obscure cases reveal what is

going on by the presence or absence of the *a* wave superimposed on the *c* or on the *v* (4) Finally true atrial standstill or paralysis either transient or complete may account for the absence of the *P* waves due to depression of the pacemaker in the sinoatrial node and to inability of the lower, that is the atrioventricular node to start an atrial contraction (see Figure 162 page 979)

Inversion of the P wave (1) Inversion of the *P* wave in Lead 2 is abnormal and occurs most commonly in the case of atrial premature beats (see Figure 154) (2) Inverted or diphasic *P* waves also occur sometimes with continuous abnormal atrial rhythms most commonly in atrial paroxysmal tachycardia (Figure 156 page 879) (3) A third cause for inversion of the *P* wave very much rarer than that due to atrial premature contractions or to atrial paroxysmal tachycardia is atrioventricular nodal rhythm already mentioned (see Figure 163) Rarely an excessive irritability of the atrioventricular junctional tissue may give rise to paroxysmal tachycardia originating there (4) A fourth cause of inversion of the *P* wave is retrogression giving rise to a so called retrograde *P* wave following a ventricular premature beat

In some instances the *P* waves are more readily studied otherwise than in Lead 2 for example in the special atrial lead with exploring electrode in the third intercostal space at the right sternal border or in an esophageal lead when the *P* waves are indistinct or not seen in other leads

THE ATRIOVENTRICULAR OR *P R* (*P Q*) INTERVAL

The *P R* (*P Q*) interval is routinely studied in Lead 2 but observations of its length in the other leads should always be made It is a measure of atrioventricular conduction time from the atrial pacemaker through the atrial muscle across the junction from the atrial myocardium to atrioventricular node through this node and the bundle leading down from it and through the right and left bundle branches and their ramifications in the Purkinje network into the ventricular muscle fibers themselves at which moment the *QRS* wave begins The *P R* interval is measured from the beginning of the upstroke of the *P* wave to the beginning of the *QRS* wave whether this be upstroke or downstroke It normally varies in the adult from 0 12 to 0 20 (or even in rare cases 0 21 or 0 22) second averaging 0 16 second and in infancy and childhood from 0 08 to 0 18 second averaging 0 12 or 0 13 second Its duration is undoubtedly a function of the heart size (Figure 53 page 207)

Some years ago it was demonstrated (White Leach and Foote 1941) that an error may arise in the measurement of the *P R* interval especially in Lead 2 due to the neutralization of *Q* and *R* waves in two of the three classical leads with resulting isoelectric onset of the *QRS* waves in the other lead thus apparently prolonging the *P R* interval This happens most commonly when a short *Q* or *R* in Lead 1 is exactly equal in amplitude and duration to a short *R* or *Q* in Lead 3 the *P R* interval in Lead 2 is then abnormally prolonged by 0 02 or 0 03 second to include the isoelectric onset of *QRS* Or

otherwise Q_1 may neutralize Q to prolong P R_3 or Q_3 may neutralize Q to prolong P R_1 In occasional cases this error is clinically important when a P R interval of 0 19 or 0 20 second is read as 0 22 second Hence careful scrutiny for this possible error is always essential A factor less important, which may erroneously shorten the *P-R* interval or neutralize the other effect is an isoelectric beginning of the *P* wave

Lengthened P R interval If the *P R* interval is over 0 21 second atrioventricular block is said to be present Only very rarely is a *P R* interval found to measure normally over 0 20 second but in a few normal adults it has apparently even reached 0 22 second The greater part of the *P R* time interval is consumed in the passage of the excitation wave through the atrioventricular node and the atrionodal junction just above it (see Chapter 34) The commonest causes of prolongation of the *P R* interval are active rheumatic myocarditis coronary heart disease and digitalis intoxication

Shortened P R interval The *P R* interval may frequently appear shortened when the atria and ventricles are beating independently as in complete heart block reciprocal rhythm or ventricular escape and in many instances of the ventricular premature beat In such cases it is better to speak of the intervals between the *P* waves and the *R* waves rather than of the *P R* interval as such True shortening of the *P R* interval is found in atrioventricular nodal rhythm when the *P* wave almost always inverted falls just before just after or with the *R* wave and in that variation of normal rhythm which consists of wide *QRS* waves with shortened *P R* intervals (of 0 1 second or less) in healthy young persons prone to paroxysmal tachycardia (Wolff Parkinson and White 1930) (see Figure 168 page 953 and Chapter 34)

THE FIRST VENTRICULAR DEFLECTION OR *QRS* WAVE

The normal *QRS* wave The *QRS* wave the first ventricular deflection of the electrocardiogram and sometimes called for short the *R* wave is in *Lead 2* a sharp spike like monophasic diphasic or triphasic complex with little or no initial downward projection known as the *Q* wave a high upward projection known as the *R* wave and a variable usually slight to moderate downward projection called the *S* wave (Figures 40 42 43 and 44) Together all components of the *QRS* complex should measure not over 0 1 second in duration This first ventricular complex (*QRS* wave) represents the rapid activation of the entire ventricular myocardium by the excitation wave as it leaves the end branches (called the Purkinje fibers) of the special intraventricular conducting mechanism below the bundle of His The terms dextrogram and levogram have been applied to records representing in experimental animals the primary spread of the excitation wave through right and left ventricles respectively the addition of dextrogram and levogram results in the record obtained from both ventricles simultaneously For the sake of convenience and uniformity it has been agreed generally to call the first upward deflection of the *QRS* wave the *R* phase or wave any downward deflection

preceding the R the Q wave any downward deflection following the R t wave and a second upward deflection following the S the R wave, if the but one deflection downwardly directed it is labeled the QS wave (Comm of Electrocardiographic Nomenclature American Heart Association 19 So far as time relations are concerned the Q of Lead 3 may coincide the R of Lead 1 and the R of Lead 1 with the S of Lead 3 the nomencl is not concerned with time relations but rather with direction above or b the baseline

The Q part of the QRS complex in *Lead 2* is usually absent or at i but a short point projecting 1 or 2 mm below the baseline except in the of infants and young children when it may form a more appreciable pa the whole QRS complex being as great as 3 or 4 mm in amplitude Th wave in Lead 2 in the normal adult varies from 5 to 35 mm in ampli and in infants from 5 to 10 mm It is sharp rarely slightly notched or slu on upstroke downstroke or peak It may be the only part of the QRS com present The S wave is usually but a slight sharp downstroke of 1 to 3 immediately succeeding the R wave in fact continuous with it, it is quently absent

In *Leads 1 and 3* the QRS waves have normally less amplitude than in l 2 When the R or S wave occurs alone it is probable that either the other c ponents are fused with it or they may be isoelectric and therefore invi in one or another lead thus resulting in an erroneous measurement of QRS duration A narrow QRS wave with isoelectric onset ending or bot most commonly found in Lead 2 where its apparent duration may in cases measure only half that of QRS_1 or QRS_3 an important error espec in the presence of bundle branch block which may be clearly evident in L 1 and 3 Thus all three leads must be carefully scrutinized not only to de mine the correct measurement of the P R interval but also to learn the QRS duration the widest QRS wave in any one of the three classical lea the correct one and so as a rule, is the shortest P R interval Frequentl Lead 3 but rarely in Lead 1 the phase of the QRS wave with the gre amplitude is normally directed downward whether Q or S

In the *unipolar limb leads* (Figures 42 43 and 44 pages 190 191 1 the QRS wave is normally inverted in Lead aVR with deep Q and smal usually upright but sometimes inverted (if the heart is very vertical) in l aVL and rarely normally inverted that is with Q wave in Lead a there may be very small R and S waves in Lead aVF if the heart lies h zontally

In the *six unipolar precordial leads* (V_1 to V_6 inclusive) the QRS wav normally diphasic with short R and deep S in the first two leads and ta and short S in the last two leads with R and S of intermediate amplitude Leads V_3 and V_4 in other words the R wave increases and the S wave creases as one moves from right to left (see Figures 42 43 and 44 pages 1 191 192) It is to be noted that in the precordial leads the peak of the R w marks the time of arrival of the intrinsic excitation wave at the muscle uni

lying the particular exploring electrode involved the larger the ventricle the later and the higher the peak while the *S* wave usually reflects the activity of the opposite ventricle *Q* waves normally are absent or small Hence since the left ventricle is normally preponderant in size the *S* waves are larger over the right ventricle (that is in the right precordial leads) and the *R* waves are larger over the left precordial leads However the position of the heart enters in and may cause on occasion a very confusing picture especially if we take into account rotation of the heart around each of its three axes (Goldberger 1947) The effects of these variations of position added to the effects of disease processes and of various physiologic and toxic states comprise an extremely complicated miscellany that will require much research completely to elucidate

Abnormalities of the *QRS* wave The *precordial leads* may show the state of different parts of the heart in particular of the right and left ventricles better than do the limb leads since they reflect in the main what is directly beneath them Thus if the right ventricle is enlarged there is a delay in the appearance of the intrinsic deflection represented by the peak of the *R* wave in Leads V and V_2 overlying the right ventricle and along with this delay frequently an increase in amplitude also If there is right bundle branch block the intrinsic deflection is still further delayed in those leads resulting in a wide bifid or M shaped complex Also if the right ventricle is enlarged there tends to be a large *S* wave in the left precordial leads over the left ventricle that is in Leads V and V_6 Either Lead V_3 or V_4 is often a transitional point sometimes directly over the interventricular sulcus and sometimes over either ventricle and at right angles to the spatial axis as such either one is commonly used in identifying the anteroposterior plane in vectorcardiography (see page 202) In obscure cases x ray examination and the limb leads can help a good deal

If the left ventricle is enlarged the *QRS* waves in Leads V_5 and V_6 are altered accordingly with delay in appearance of the peak of the *R* wave (intrinsic deflection) higher amplitude of the *R* wave and in Leads V and V_2 over the right ventricle increased *S* waves Here again displacement or rotation of the heart to the right gives much more evidence of the left ventricle in the precordial leads than usual and may be misleading In left bundle branch block there is a much delayed intrinsic deflection peak in Leads V and V_6 often giving an M shape

The enlargement of the heart that affects the precordial *QRS* wave especially is that due to hypertrophy dilatation also has an effect on the duration of the *QRS* wave but manifests itself more on the *S T* segment and *T* wave because of the abnormal myocardial condition

It is also important to note that normally the bigger the heart the wider the *QRS* wave without the need of postulating any abnormal delay in i v conduction Thus the human infant s *QRS* wave is but 0 05 second wide normally the human adult s 0.10 second while the normal adult elephant s *QRS* wave is 0 20 second in duration (Figure 54) it would seem likely that the adult whale s *QRS* wave should be 0 4 second wide Thus hypertrophy alone

undoubtedly gives rise to slightly increased *QRS* duration even up to 0 11 second without bundle branch block per se

Absence of the R wave leaving only a QS complex is an important residual effect of a myocardial infarct underlying the particular precordial lead concerned This finding when present is a significant clue differentiating myocardial infarction from other conditions that may produce abnormal precordial *T* waves

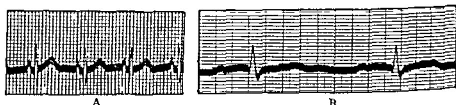


FIG 54 (*A*) Electrocardiogram (Lead 2) of a normal newborn infant B B showing the very short time intervals *P R* *QRS* and *Q T* (*B*) Electrocardiogram of a normal middle aged elephant M showing the very wide time relations a function of the size of the elephant s heart in contrast to the time intervals of the infant s electrocardiogram The speed of the film is the same in both (*A*) and (*B*)

An important observation that should be added concerns the amplitude of the *QRS* wave in the precordial leads Of equal importance with actual ventricular size is closeness of the lead to the heart Thus a thin chest wall will result in greater amplitude while a thick (e g obese) chest wall or fluid will decrease the amplitude

In the *unipolar limb leads* position of the heart is particularly reflected in the *QRS* waves as well as is heart disease In general a deep *S* wave in Lead aVR goes with left ventricular preponderance and a horizontal heart position *while a high R wave in Lead aVF goes with left ventricular preponderance* and a vertical heart position a *Q* wave is normally encountered but rarely in Lead aVF and an absence of *R* wave means a serious myocardial defect (an electrical hole facing the lead point usually due to infarction)

Finally in the old classical bipolar limb leads despite the concentration of interest in these leads in earlier editions of this book little can really be said about abnormalities of the *QRS* waves because of the wide range of the normal and the striking effect of varying positions of the heart Thus the great bulk of instances of so called right and left axis deviations is of physiologic interest only associated primarily with heart position although there are cases of course, of extreme degree of really significant axis deviation as in the case of the tetralogy of Fallot or of the atrial septal defect Also deep *Q* waves in Lead 1 are abnormal usually signifying anterior myocardial infarcts and especially prominent *Q* waves in Leads 2 and 3 generally mean posterior myocardial infarcts And of course *QRS* waves over 0 12 second wide mean bundle branch block but it is not always so easy as we used to think to tell right from left branch blocks in these leads alone There are exceptions that are *properly revealed only in the precordial leads which should always be*

taken anyway in cases with widened *QRS* waves As a rule it is true that wide upright *QRS* waves in Lead 1 and wide inverted *QRS* waves in Lead 3 mean left bundle branch block the reverse being true for right bundle branch block The last chapter in the book will have more to say about this

The term *low voltage* has been applied to the *QRS* wave in particular when it has extremely small amplitude either above or below the baseline At one time 5 mm that is 0 05 mv was arbitrarily selected as the borderline of normal Inasmuch however as normal individuals have shown amplitudes either above or below the baseline of the limb leads of 4 to 5 mm (0 4 to 0 5 mv) it is better to restrict the term low voltage to amplitudes of the *QRS* wave of 3 mm (0 3 mv) or less especially if the low voltage involves the *T* and *P* waves too Such low voltage has been noted in several conditions in particular in cases of diffuse myocardial disease due to coronary atherosclerosis or other cause extensive pericarditis acute or chronic and rare factors as yet unexplained In such cases the precordial leads generally show fair amplitude of the *QRS* waves but in a few instances they too may be much reduced and when they are the causative abnormal conditions are usually of greater degree The voltage however of the *QRS* waves in the precordial leads is affected also by distance of the electrode from the heart Thus an extensively fat chest wall or much fluid or air interposed between the heart and chest wall are factors that reduce the precordial *QRS* voltage

Alternation of the amplitude of the QRS waves without other change (that is without alternating change of shape or of time interval) is exceedingly rare I have seldom encountered it in the past 30 years A few years ago two cases were reported the first case being the only one found in a series of approximately 10 000 electrocardiograms taken over a period of 13 years (Hamburger Katz and Saphir 1936) the prognosis is apparently bad as in the ca e of the ordinary pulsus alternans On the other hand alternation of the arterial pulse is common and is attended in only the rarest cases by electrocardiographic alternation either of *QRS* waves or *T* waves or both

THE *S T* SEGMENT

Immediately following the onset of systole that is after the *QRS* wave there is usually in the normal subject a short isoelectric interval showing itself electrocardiographically as the *S T segment following the S T junction* Both the segment between the *S* and the *T* waves and that of the *T* wave itself are easily susceptible to modifying influences physiologic effects structural changes anoxia and myocardial infection and poisoning which may produce changes of shape and amplitude The *S T* segment and the *T* wave represent simply phases of the same electric process repolarization during cardiac systole The *S T* junction and *S T* segment may be normally slightly elevated up to 1 mm in limb leads and to 2 mm in precordial leads

Changes in the S T segment There are frequent changes in the *S T* segments which accompany abnormalities of the *T* waves themselves but which

actually may be more important in the information they yield about the myocardium they are as a rule temporary however subsiding when toxic influences and currents of injury subside The most common and most striking S T segment abnormalities are those associated with digitalis intoxication and with myocardial infarction and ischemia (most commonly from coronary disease rarely from trauma or a state of vascular shock or anoxia) acute pericarditis with its associated subpericardial myocardial involvement may elevate the S T segments appreciably especially in Leads 1 and 2 and in the precordial leads involved With full digitalization the S T segment of Leads 1 2 and 3 and of the multiple precordial leads is considerably depressed and is said to sag dropping sometimes several millimeters below the base line so that the T may arise very low and be diphasic or in extreme cases totally inverted (see Chapter 30) This digitalis effect is in contradistinction to the findings in acute myocardial infarction and ischemia when the S T segments are depressed or raised from the baselines in the opposite direction to the T wave changes that is early in the anterior wall type of infarction the S T segment is elevated in Leads 1 V_4 and V and depressed in Lead 3 and vice versa in posterior wall infarction type these changes are transient, persisting as a rule but a few hours or days (see Chapter 21) The S T segment tends to be markedly elevated in the multiple precordial leads over the region of the fresh anterior infarct while it may be considerably depressed in cases of acute posterior infarction (see Chapter 21) Also injury at the endocardial surface of the left ventricle may cause depression of the S T segments in the precordial leads over the left ventricle in contrast to the effect of the more usual subpericardial lesions In the case of large chronic myocardial infarcts usually associated with cardiac aneurysms the S T segments may be permanently displaced (e g elevated in Leads 1 V_4 and V_6 in the case of large anterior aneurysms)

Infectious changes other toxic poisoning of the myocardium and hyperventilation may sometimes affect the S T segment but rarely as much as does acute infarction or digitalization hypothyroidism has but little effect on the S T segment while flattening out the T waves In some cases of left ventricular enlargement (or strain) there is a slight depression of the S T segment in Lead 1 even when there is no left axis deviation (Barnes 1940) In fact it is now well recognized that S T segment depression in Lead 1 and in Leads V_4 and V is more characteristic of the effects of strain on the left ventricle than is left axis deviation this simulates the effect of anoxia in acute coronary insufficiency

THE SECOND VENTRICULAR COMPLEX OR *T* WAVE

The normal *T* wave The *T* wave or second ventricular wave of the normal electrocardiogram is in Lead 2 a blunt rounded upright deflection following the S T segment beginning gradually from the isoelectric baseline a short but variable distance about 0 05 to 0 15 second after the end of the QRS wave rising to a height of 2 to 10 mm usually 3 or 4 and sloping somewhat more

sharply downward to the baseline again to end about 0 25 to 0 30 second after the end of the normal *QRS* wave (Figures 42 43 and 44) The duration or width of the *T* wave thus varies greatly from about 0 10 to 0 25 second It falls during ventricular systole ending with the end of systole and the occurrence of the second heart sound It has been variously explained probably best as the repolarization (recharging) of the myocardium as contrasted with the depolarization (electric discharge) of the myocardium represented by the *QRS* wave The *T* waves in Leads 1 and 3 are normally of less amplitude as a rule than the *T* wave T_1 is low (about 1 or 2 mm) but almost invariably upright normally while T_3 also of low amplitude may be normally upright flat, or even inverted The *T* waves in the unipolar limb leads vary from normally inverted in aVR to upright or inverted in aVL and aVF depending on the position of the heart tending to be inverted in aVL and upright in aVF in the case of a vertical heart and upright in aVL and low but not inverted in aVF in the case of a horizontal heart The *T* wave in precordial Leads V_3 to V_6 inclusive is almost always upright (about 3 to 6 mm) in the normal adult but in the young child it may be inverted normally The *T* waves vary from very low flat or inverted in V_1 with increasing amplitude to high (5 to 10 mm) in V_3 and V_4 to lower levels in V and V_6 they should not normally be inverted in the adult except in V_1 and V

Physiologic variations of the T wave As stated above the *T* waves in Lead 3 normally vary widely from upright to inverted depending in large part on position of the heart as affected by the height of the diaphragm in opposite phases of respiration and in opposite body builds thus in full inspiration and in the case of a vertical heart the *T* waves in Lead 3 tend to be upright in direction with a swing of the electric (and anatomic) axis toward the right while in full expiration and in the case of a horizontal heart the *T* waves in Lead 3 tend to be inverted with a swing of the axis toward the left (see Figure 4 page 33)

Until recent years however flattening or inversion of the *T* waves in Leads 1 2 and V_3 to V_6 in the adult has been attributed to actual heart disease In Leads 1 and V_4 and V such a surmise is almost invariably correct so far as we yet know with very rare exceptions due to the same factors namely heart position and autonomic nerve influences which can be responsible in the case of the far more numerous exceptions found in Lead 2

Occasionally flattening notching or even inversion of the *T* waves in Lead 2 may be a positional effect in normal individuals in such cases a vertical heart position in a long thorax with tendency to right axis deviation is attended in the sitting or standing position by notched diphasic or inverted *T* waves which assume the usual normal upright appearance in the recumbent position or on deep expiration (with or without much of any change in axis deviation of the *QRS* waves on changing position rotation of the heart probably playing the important role) It is important to recognize this normal variation which has frequently in the past been attributed to myocardial disease (see Figures 5 and 6 page 34 and page 35) (White Chamberlain and Graybiel 1941) In very rare cases even T_1 may be normally inverted when the heart is

unusually placed vertically with the *T* in aVL deeper than in aVR or horizontally with marked clockwise rotation

In addition to the effect of position autonomic nerve impulses may affect the *T* waves in Lead 2 Sympathetic stimulation as *during* exercise and from fear or adrenaline and vagal inhibition as from atropine lower the *T* waves even to the point of inversion (Figure 55) (Hartwell et al 1942), while

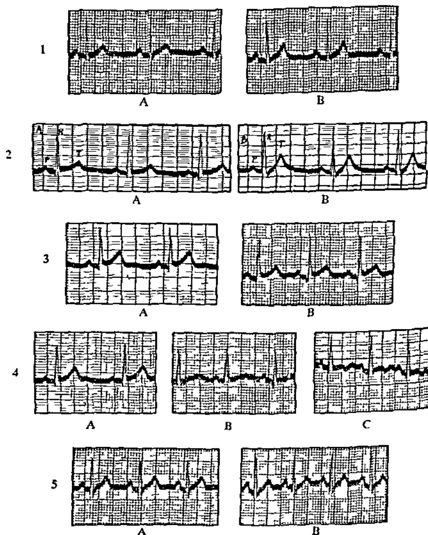


FIG 55 Changes in the *T* waves of the electrocardiogram resulting from the action of certain drugs in particular ergotamine atropine and adrenaline and of exercise (during and after) Note the increase in the *T* waves by vagus stimulation as evidenced by (1) the action of ergotamine and (2) the after-effect of exercise and the depression of the *T* waves as the result of sympathetic nerve stimulation or preponderance as evidenced by the effect of (3) atropine (4) adrenaline and (5) exercise itself directly All tracings are of Lead 2 (*A*) control record (*B*) records at height of effect (*C*) shows maximal adrenaline effect—drug given intravenously (Hartwell Burrett Graybiel, and White *J Clin Investigation* 1942 XXI 409)

vagal stimulation as from ergotamine and *after* exercise raises the *T* waves (Figure 55)

Abnormalities of the *T* wave *Increase in amplitude of the T wave* The end of the *T* wave of Lead 1 tends to become higher in cases of posterior myocardial infarction due to coronary thrombosis in contrast to late inversion of the *T* wave in Lead 3 while the reverse is true that is there is a late increased elevation of T_3 when there is late inversion of T_1 in the cases of anterior wall infarction In the old Lead 4 and in the multiple precordial leads over the left ventricle V_4 V and V_6 the *T* may remain unchanged or become higher than normal in the posterior wall infarction it is almost always considerably inverted in the anterior wall infarction (see Chapter 21) especially in chest Leads V_4 V and V_6 In cases of lateral wall infarction it may be inverted in Lead V_6 only

In the electrocardiograms of premature beats marked axis deviation and bundle branch block the *S T* segment and *T* wave are usually widely deviated from the baseline in the opposite direction from that of the abnormal *QRS* wave thus giving sometimes very high *T* waves A similar opposite direction of *T* wave from *QRS* wave in Leads 1 and 3 helps to separate the marked axis deviation due to pathologic cardiac conditions from left axis deviation of lesser degree which may be due to change in position of the heart (when the *T* wave tends to take the same direction from the baseline as does the *QRS* wave) Thyrotoxicosis sometimes stated to show a *T* wave increase is as a matter of fact generally without appreciable effect or has an opposite effect even to flatten or invert the *T* wave doubtless due to the sympathetic overstimulation

Decrease in amplitude and inversion of the T wave Decrease in amplitude of the *T* waves from the normal and their inversion in disease are found under several conditions In Lead 2 decrease in amplitude is frequently present in marked left or right axis deviation or even in right or left bundle branch block along with a diphasic character of the *QRS* wave due to the neutralizing effect of Leads 1 and 3 on each other In general however flattening and inversion of the *T* waves in the three classical leads are most commonly the result of digitalis action of myocardial ischemia or infarction from coronary disease of acute pericarditis or chronic constrictive pericarditis of infectious myocardial involvement and of hypothyroidism (myxedema or cretinism) There are differences between the effects of these five clinical conditions In the multiple precordial leads the *T* waves vary according to the part of the heart affected but are influenced like the limb leads by general factors such as digitalis myocarditis and myxedema

1 Digitalization usually causes a decrease leading to flattening or even in extreme cases to deep inversion of the *T* wave following a sagging of the *S T* segment (see Figure 158 page 897 and Chapter 30)

2 The *T* wave of myocardial ischemia or infarction due to coronary disease or insufficiency tends to be flattened or inverted in Lead 2 but varies in the other leads according to the site of the maximum amount of myocardial

change It is at first slightly elevated along with the S T segment, in Lead 1 with or without very slight late inversion (Pardee s sign Pardee 1920) during the most acute stage of anterior wall type of myocardial infarction (due probably to a current of injury at the left ventricular apex) but it becomes usually sharply inverted after a few days remaining inverted for weeks, months or years When there is chronic coronary insufficiency with or without actual old infarction involving a large area of the left ventricle toward the apex the T waves in Leads 1 and V_4 and V_5 are usually flattened or inverted in their terminal portions In cases of anterior wall myocardial infarction or left ventricular basal ischemia the same statements just made concerning T_1 apply to the T waves in Lead 3 instead In the multiple precordial leads the T waves are unchanged or heightened in the case of the posterior wall infarction or left basal ischemia and flattened or inverted (often deeply so) over the left ventricle in the case of anterior infarction or left apical ischemia When there are multiple areas of infarction or ischemia there are multiple effects on the electrocardiogram which are often confusing perhaps the simplest combination is inversion of the T waves in Leads 1 2 and 3 with diphasic T waves in the precordial leads over the left ventricle when there are comparable infarcts at both apex and base (see Chapter 21)

In the multiple precordial leads inversion of the T waves over the right side of the precordium and not over the left indicate enlargement of or damage to the right ventricle or infarction of the interventricular septum while inversion of the T waves over the extreme left side of the precordium indicate infarction or other damage of the lateral wall of the left ventricle

3 With pericarditis especially when there is acute or chronic constriction of the heart and great vessels the T waves tend to become flattened or more often inverted in all leads after temporary elevation of the S T segments but especially in Leads 1 and 2 for some days in the early stages (see Chapter 27)

4 With serious infections there are occasionally observed changes in the T waves consisting of decrease in amplitude flattening or inversion in both limb leads and multiple precordial leads similar to those just recounted as sometimes occurring in pericarditis these changes are due to acute myocardial involvement and are particularly likely to occur in rheumatic fever diphtheria and pneumonia and sometimes in virus diseases The same effects are due rarely to noninfectious poisons (other than digitalis which has been mentioned above) as from tobacco (see Chapter 23)

5 The T waves of hypothyroidism are very low absolutely flat (most commonly) or even inverted in all leads they resume a normal amplitude after thyroid therapy (see Chapter 18)

There are other rare instances of depression or inversion of the T waves of uncertain or unknown nature and even an individual who is apparently normal may temporarily show this finding due as a rule to unusual heart position or nerve influence (see Figures 5 page 34 and 55 page 218 for example)

The *T* wave is frequently diphasic but rarely notched Its diphasic character results often from the inverted nature of the *S T* segment which merges into the slightly upright *T* wave as in digitalis action occasionally the diphasic sequence is the reverse first upright then inverted as in cases of cardiac infarction A late notch or dip in a low *T* wave in Lead 2 suggests the effect of heart position in an otherwise normal person in the sitting position in such a case a further electrocardiogram should be taken with the subject recumbent or in full expiration to correct the effect of the heart s unusual angle or rotation

Alternation of the *T* waves in amplitude alone like alternation of the *QRS* waves is very rare it may accompany alternation of the arterial pulse as a serious sign

THE *Q T* DURATION

The time interval from the onset of the *QRS* wave to the end of the *T* wave can be taken to measure quite accurately the duration of ventricular systole when the deflections are clearly marked so that the end points are readily seen With good technic this so-called *Q T* duration of the electrocardiogram is the best measure we possess for the length of systole With clear curves measurement by the Lucas comparator gives an error under 0 01 second The *Q T* duration (duration of systole) varies primarily with the heart rate being shorter with faster rates and longer with slower rates about 0 35 second at a heart rate of 75 0 25 second at a rate of 120 and 0 45 second at a rate of 45 The *Q T* duration varies abnormally only in some cases with high grade atrioventricular and intraventricular block in ventricular premature beats in hypocalcemia and hypopotassemia and with marked enlargement (especially dilatation) of the heart in which conditions it is longer than the outer limit of the normal in heart failure a prolonged *Q T* duration (systole) is shortened by an adequate digitalis effect With respect to heart size it is of considerable interest that the duration of systole (the *Q T* duration) of the elephant s heart is relative to heart rate much longer than that of the human heart (White Jenks and Benedict 1938) (Figure 54 page 214) and one might justly prophesy that the whale s *Q T* duration like other time intervals would be similarly relatively prolonged

THE *U* WAVE

Occasionally in Leads 1 and 2 and frequently in the precordial leads there occurs normally a slight upright deflection a small wave usually less than 1 mm high but sometimes higher immediately following the *T* wave and therefore appearing in early diastole (Figures 40 42 44 and 53) This is called the *U* wave Its significance is unknown but it is probably representative of some diastolic electric process in the myocardium since it is more evident after a high or deep *T* wave than at other times and since it tends to be inverted when the *T* wave is inverted The *U* wave is apparently of little clinical

importance except that it may be abnormally inverted when the *T* wav upright and that it may be confused with the *P* wave or more commonly the end of the *T* wave in which latter case it may be wrongly interpreted notching of the *T* such an error can be avoided by a measurement of expected *Q T* interval at the heart rate recorded

Serial electrocardiograms In closing this chapter I would like to emph the great importance of serial electrocardiography Repeated records are c essential for the diagnosis of such acute conditions as myocardial infarc acute pericarditis and the acute cor pulmonale Annual monthly wee daily or even hourly records may reveal much more than any single elec cardiogram Also every young person while in good health should hav routine electrocardiogram taken for future reference just as he or she sh also have a chest x ray film

BIBLIOGRAPHY

ELECTROCARDIOGRAPHY

SEE ALSO REFERENCES UNDER CHAPTER 12 TO 20 INCLUSIVE AND FOLLOWIN CHAPTERS 31 PREMATURE BEATS AND PAROXYSMAL TACHYCARDIA 3? ATRIAL FIBRILLATION AND ATRIAL FLUTTER QUINIDINE THERAPY AND 33 HEART BLOCK

American Heart Association Second Supplementary Report by the Committee for Standardization of Precordial Leads *Am Heart J* 1943 XXV 535

Ashman R and Byer E "The Normal Human Ventricular Gradient I Factors W Affect Its Direction and Its Relation to the Mean QRS Axis *Am Heart J* 1 XXV 16

II Factors Which Affect Its Manifest Area and Its Relationship to the Man Area of the QRS Complex *Ibid* 1943 XXV 36

Ashman R and Hull E *Essentials of Electrocardiography* Macmillan Co New Y 2nd ed 1941 (1st ed 1937)

Barker P S Macleod A G Alexander J and Wilson F M "The Excita Process Observed in the Exposed Human Heart *Tr A Am Physicians* 19_9 XI 125 and *Am Heart J* 1930 V 720

Barnes A R *Electrocardiographic Patterns Their Diagnostic and Clinical Significa* Charles C Thomas Publisher Springfield Ill 1940

Bayliss W M and Starling E H On the Electromotive Phenomena of the Mamma Heart" *Internat Monatsschr f Anat u Physiol* 1892 IX 256

Bernstein P and Mann H Clinical Evaluation of Fetal Electrocardiography St of 100 Cases by New Technic and Improved Instrument *Am J Obst & Gyn* 194_ XLIII 21

Carter E P Richter C P and Greene C H A Graphic Applica ion of the Princ of the Equilateral Triangle for Determining the Direction of the Electrical Axis of Heart in the Human Electrocardiogram" *Bull Johns Hopkins Hosp* 1919 XXX J

Cohn A E Fraser F R and Jamieson R A "The Influence of Digitalis on the Wave of the Human Electrocardiogram" *J Exper Med* 1915 XXI 593

Craib W H The Electrocardiogram *Medical Research Council Special Report Ser* No 147 London 1930

Einthoven W "Ein neues Galvanometer" *Annalen der Physik* Folge IV 1903 \ 1059

Einthoven W Fahr G and de Waart A "On the Direction and Manifest Size of the Variations of Potential in the Human Heart and on the Influence of the Position of the Heart on the Form of the Electrocardiogram *Pflugers Arch f d ges Physiol* 1913 CL 275 Translated by Hoff H E and Sekelj P *Am Heart J* 1950 XL 163

Feil, H "The Auricular Wave (P) of the Human Electrocardiogram in Normal and Pathological States *J Mt Sinai Hosp* 1942 VIII 502

Fridericia L S Die Systolendauer im Elektrokardiogramm bei normalen Menschen und bei Herzkranken I Beziehung zwischen der Pulsfrequenz und der Dauer des Ventrikelelektrokardiogramms bei normalen Menschen in der Ruhe *Acta med Scandinav* 1920-21 LIII 469

Galvani L *De viribus electricitatis in motu musculari commentarius* Istituto delle scienze di Bologna 1791 VII

Goodyer A V N Geiger A J and Monroe W M Clinical Fetal Electrocardiography *Yale J Biol & Med* 1942 XV 1

Hamburger W W Katz L N and Saphir O Electrical Alternans A Clinical Study with a Report of Two Necropsies *J A M A* 1936 CVI 902

Hartwell A S Burrett, J B Graybiel A and White P D "The Effect of Exercise and of Four Commonly Used Drugs on the Normal Human Electrocardiogram with Particular Reference to T Wave Changes *J Clin Investigation* 1942 XXI 409

Hecht H H 'The Influence of the Indifferent Electrode Upon the Precordial Electrocardiogram" *Am Heart J* 1942 XXIV 529

Herrmann G and Schwab E H Some Experimental and Clinical Electrocardiographic Observations on R S T and T Changes in Pericarditis *Tr A Am Physicians* 1934 XLIX 229

Katz L N *Electrocardiography* Lea & Febiger Philadelphia 1941

Exercises in Electrocardiographic Interpretation Lea & Febiger Philadelphia 1941

Katz, L N et al "The Diagnostic Value of the Electrocardiogram Based on the Analysis of 149 Autopsy Cases *Am Heart J* 1942 XXIV 627

Kisch B Nahum L H and Hoff H E The Predominance of Surface Over Deep Cardiac Injury in Producing Changes in the Electrocardiogram" *Am Heart J* 1940 XX 174

Kolliker A and Muller H "Nachweis der negativen Schwankung des Muskelstroms am naturlich sich contrahirenden Muskel *Verhandl d physik med Gesellsch i Wurzburg* 1856 VI 528

Kraus F and Nicolai G *Das Elektrokardiogramm des gesunden und kranken Menschen* Veit Leipzig 1910

Lewis T *The Mechanism and Graphic Registration of the Heart Beat* Shaw and Sons Ltd London 3rd ed 1925 (1st ed 1911)

Mainzer F and Krause M 'The Influence of Fear on the Electrocardiogram *Brit Heart J* 1940 II 221

Mann H A Method of Analyzing the Electrocardiogram *Arch Int Med* 1920 XXV 283

"The Monocardiograph" *Am Heart J* 1938 XV 681

Marcel M P and Exchaquet J P L electrocardiogramme du foetus humain *Arch d mal d coeur* 1938 XXXI 504

Matteucci C Sur le courant electrique des muscles des animaux vivantes ou recemment tu s *Compt rend d l Acad d sc* 1843 XVI 197

Nahum L H and Hoff H E 'The Interpretation of the U Wave of the Electrocardiogram *Am Heart J* 1939 XVII 585

Pardee H E B An Electrocardiographic Sign of Coronary Artery Obstruction" *Arch Int Med* 1920 XXVI 244

Clinical Aspects of the Electrocardiogram Paul B Hoeber Inc New York 4th ed 1941 (1st ed 1924)

Parkinson, J and Bedford D E Successive Changes in the Electrocardiogram After Cardiac Infarction (Coronary Thrombosis) *Heart* 1928 XIV 195

Rykert H E and Hepburn J "Electrocardiographic Abnormalities Characteristic of Certain Cases of Arterial Hypertension" *Am Heart J* 1935 X 942

Samojloff A and Steshinsky M Ueber die Vorhoferhebung des Elektrokardiogramms bei Mitralstenose *Munch med Wchnschr* 1909 LVI 1942

Sanderson J B and Page F J M On the Time Relations of the Excitatory Process in the Ventricle of the Heart of the Frog *J Physiol* 1880 II 384
Sigler L Electrocardiographic Changes with Alterations of Posture from Recumbent to Standing Positions *Am Heart J* 1938 XV 146
Smith F M "The Ligation of Coronary Arteries with Electrocardiographic Study *Arch Int Med* 1918 XXII 8
Waller A D A Demonstration on Man of Electromotive Changes Accompanying the Heart s Beat *J Physiol* 1887 VIII 229
White P D Chamberlain F L and Graybiel A Inversion of the T Waves in Lead II Caused by a Variation in Position of the Heart *Brit Heart J* 1941 III 233
White P D Jenks J L Jr and Benedict F G The Electrocardiogram of the Elephant *Am Heart J* 1938 XVI 744
White P D Leach C E and Foote S A "Errors in Measurement of the P R (P-Q) Interval and QRS Duration in the Electrocardiogram *Am Heart J* 1941 XXII 321
White P D and Mudd S G Observations on the Effect of Various Factors on the Duration of the Electrical Systole of the Heart as Indicated by the Length of the Q-T Interval of the Electrocardiogram *J Clin Investigation* 1929 VII 387
Wilson F N "The Distribution of the Potential Differences Produced by the Heart Beat Within the Body and at Its Surface *Am Heart J* 1930 V 599
Wilson F N Macleod A G and Barker P S *The Distribution of the Currents of Action and of Injury Displayed by Heart Muscle and Other Excitable Tissues* University of Michigan Press Ann Arbor 1933
Wise N B Comeau W J and White P D "An Electrocardiographic Study of Twins *Am Heart J* 1939 XVII 701
Wolff L Parkinson J and White P D Bundle Branch Block with Short P R Interval in Healthy Young People Prone to Paroxysmal Tachycardia *Am Heart J* 1930 V 685
Wood F C and Wolferth C C An Electrocardiographic Study of Coronary Occlusion The Inadequacy of the Three Conventional Leads in Recording Certain Characteristic Changes in Action Currents *J Clin Investigation* 1932 XI 815

Recent References (1944–1950)

Abildskov J A Burch G E and Cronvich J A 'The Validity of the Equilateral Tetrahedron as a Spatial Reference System *Circulation* 1950 II 122
Bayley R H The Electrocardiographic Effects of Injury at the Endocardial Surface of the Left Ventricle *Am Heart J* 1946 XXXI 677
Benjamin J M Jr Schwan H Kay C F and Hafkenschiel J H The Electrical Conductivity of Living Tissues As It Pertains to Electrocardiography I Review of the Problem of Homogeneity vs Nonhomogeneity an Outline of the Technical Aspects of Tissue Resistivity Measurements and a Critical and Experimental Analysis of Certain Pertinent Experiments" *Circulation* 1950 II 321
Burch G E and Winsor T *A Primer of Electrocardiography* Lea & Febiger Philadelphia 2nd ed 1949 (1st ed 1945)
Dressler W and Roesler H *An Atlas of Electrocardiography* Charles C Thomas Publisher Springfield Ill 1949
Duchosal P and Sulzer R La Vectorcardiographie S Karger *Bale (Suisse)* 1949
Franke H and Gebert E Über die asynchrone Erregung der Vorhofe im intrakardialen Ekg beim gesunden Organismus" *Ztschr f Kreislauff* 1950 XXXIX 513
Goldberger E "An Interpretation of Axis Deviation and Ventricular Hypertrophy *Am Heart J* 1944 XXVIII 621
"The Validity of the Einthoven Triangle Hypothesis" *Am Heart J* 1945 XXIX 369
Unipolar Lead Electrocardiography Lea & Febiger Philadelphia 1947
Goldman S Vivian W E Chien C K and Bowes H N "Electronic Mapping of the Activity of the Heart and the Brain *Science* 1948 CVIII 720
Grant R P "An Approach to the Spatial Electrocardiogram *Am Heart J* 1950 XXXIX 17
Grant R P and Estes E H *The Interpretation of the Electrocardiogram by Vector Methods* Blakiston Co., Philadelphia and Toronto 1951

Graybiel A McFarland R A Gates D C and Webster F A "Analysis of the Electrocardiograms Obtained from 1 000 Young Healthy Aviators *Am Heart J*, 1944 XXVII 524

Graybiel A and White P D *Electrocardiography in Practice* W B Saunders Co Philadelphia, 2nd ed 1946 (1st ed 1941)

Grewin, K E *Some Supplementary Leads in Clinical Electrocardiography with Special Regard to Electrode Placement Normal Range and Routine Applicability of Certain Chest Leads* Ivar Haeggstroms Boktryckeri AB Stockholm 1948

Hecht H H "Potential Variations of the Right Auricular and Ventricular Cavities in Man. *Am Heart J* 1946 XXXII 39

Hein G E and Reavis J C "Direct Electrocardiograms from the Human Heart in Situ Direct Leads with Precordial Leads *Circulation* 1950 I 964

Holter N J and Gengerelli J A "Remote Recording of Physiological Data by Radio" *Rocky Mountain M J* 1949 XLVI 747

Hunzicker W J and Levine H D "Clinical Evaluation of Direct Writing Electrocardiography *Am J M Sc* 1949 CCXVIII 37

Hurst J W and Doyle J T *Atlas of Vectorcardiography* In press 1951

Kanatsoulis A "Téle electrocardiographe" *I Congrès Mondial de Cardiologie Paris* Sept 3–9 1950 J B Bailliere et Fils 1950

Kistin, A D Brill W D and Robb G P Normal Esophageal and Gastric Electrocardiograms Description Statistical Analysis and Bearing on Theories of Electrocardiographic Position *Circulation* 1950 II 578

Langner P H Jr and Atkins J P "Intrabronchial Electrocardiography A Preliminary Report" *Circulation* 1950 II 419

Lenègre J and Maurice P "La derivation directe intracavitaire des courants electriques de l oreillette et du ventricule droits" *Paris med* 1945 XXXV 23 and *Arch d mal d coeur* 1945 XXXVIII 298

Lepeschkin E Zur Standardisierung der Brustwandableitungen des Ekg *Ztschr f Kreislauff* 1949 XXXVIII 9

Electrocardiographic Observations on the Mechanism of the Electrical Alternans of the Heart *Cardiologia* 1950 XVI 278

Levine H D Hellems H K Wittenborg M H and Dexter L "Studies in Intracardiac Electrography in Man I The Potential Variation in the Right Atrium" *Am Heart J* 1949 XXXVII 46

Levine H D Hellems H K Dexter L and Tucker A S II The Potential Variations in the Right Ventricle" *Am Heart J* 1949 XXXVII 64

Littmann D "Abnormal Electrocardiograms in Absence of Demonstrable Heart Disease" *Am J Med* 1948 V 337

Myers G B "The Form of the QRS Complex in the Normal Precordial Electrocardiogram and in Ventricular Hypertrophy" *Am Heart J* 1950 XXXIX 637

Myers G B and Klein, H A "The Relation of Unipolar Limb Leads to Precordial and Esophageal Leads" *Am Heart J* 1948 XXXV 727

Riseman J E F *P Q R S T A Guide to Electrocardiogram Interpretation* Macmillan Co New York 2nd ed 1947 (1st ed 1944)

Sodi Pallares D *Nuevas Bases de la Electrocardiografia* Edicion del Inst Nacional de Cardiol de Mexico 2nd ed 1949 (1st ed 1945)

Stewart C B and Manning, G W "A Detailed Analysis of the Electrocardiograms of 500 R C A F Aircrew" *Am Heart J* 1944 XXVII 502

Wilson F N et al "The Precordial Electrocardiogram" *Am Heart J* 1944 XXVII 19

"The Substitution of a Tetrahedron for the Einthoven Triangle" *Am Heart J* 1947 XXXIII 594

Wolferth C C and Livezey M M A Study of Methods of Making So-Called Unipolar Electrocardiograms *Am Heart J* 1944 XXVII 764

Wolff L *Electrocardiography Fundamentals and Clinical Application* W B Saunders Co Philadelphia 1950

Wosika P H Feldman E Chesrow E J and Myers G B "Unipolar Precordial and Limb Lead Electrocardiograms in the Aged" *Geriatrics* 1950 V 131

CHAPTER 10

OTHER METHODS OF EXAMINATION

INTRODUCTION

The patient s history physical examination electrocardiogram and roentgen ray study have been discussed in the earlier chapters of this book and have been roughly appraised in value as parts of the complete clinical examination in the order of about 45 25 15 and 10 per cent respectively These percentages add up to 95 leaving the remaining 5 per cent to be divided up among all the other methods of examination which include the technic of cardiac catheterization and the testing of blood urine strength and endurance vital capacity and other respiratory functions blood flow circulation rate and work of the heart and of the pulse Various other tests of less immediate or routine cardiovascular importance such as the basal metabolic rate and sputum and gastrointestinal examinations are not included in this chapter but are referred to later in appropriate chapters Any one of these methods of examination may however uncover a vital clue, and so they must all be borne in mind and turned to at once in case of need Many of the additional tests such as ballistocardiography the discussion of which has been transferred to a more appropriate chapter (Chapter 8) are of much academic interest and worthy of use in special investigations a few may some day assume practical importance in clinical medicine related to the heart and great vessels As a whole however at the present time the methods discussed in this chapter are infrequently of prime importance in cardiovascular diagnosis although they may be invaluable in the execution of special research

CARDIAC CATHETERIZATION

Forssmann W "Die Sondierung des rechten Herzens (Sounding the Right Heart ") *Klin Wchnschr* 1928 VIII 2085 *

* Shortly after the publ ation of this paper Dr Forssmann s attention was called to an earlier publication on catheterization of arm veins in the human for the purpose of therap (Bleichroder Unger and Loeb Intraarterielle Therap e" *B l Kl n W schr* 191_) However this earl er work apparently did not include catheterizat on of the heart per se and was not followed up by further research or application

Following the successful investigations in the cadaver I undertook the first study in living man in the form of a *research on myself* Next I arranged in a pre liminary test to have my right elbow vein punctured with a thick needle by a colleague who kindly placed himself at my disposition for this purpose I intro duced then as in the case of the researches on the cadaver a well oiled ureteral catheter of 4 Charrieres thickness through a cannula into the vein The catheter allowed itself to be introduced very easily to a length of 35 cm Since going further seemed too dangerous to the colleague we stopped the investigation at that point even though I myself felt quite well After a week I undertook a further investiga tion alone Since a puncture of the vein with a thick needle on my own body was technically too difficult I made under local anesthesia a venesection in my left elbow and introduced the catheter without any resistance in its whole extent of 65 cm This length appeared to me after measuring the surface of the body to agree with the distance from the left elbow to the heart On introduction of the catheter I had during the procedure merely a feeling of slight warmth in the wall of the vein similar to the sensation after intravenous injection of calcium chloride On backward movement the catheter touched the upper and lower wall of the subclavian vein I then felt an especially intensive warmth behind the collar bone under the insertion of the sternocleidomastoid Simultaneously doubtless through the stimulation of the vagus branches I felt a slight tendency to cough

The position of the catheter I confirmed *in a Rontgen photograph* and observed the shadow of the catheter itself by means of a mirror held by a sister before the fluoroscopic screen (Translation by myself)

Thus in 1929 Forssman successfully catheterized his own heart by way of an arm vein Considered a bold and dangerous procedure at first it has in the last few years become a commonplace though still a delicate method of study of the right heart chambers and pulmonary arterial circulation particularly in congenital cardiovascular disease and in measurement of the pulmonary blood pressure a longfelt want now at last realized (Figure 56) It is very im portant wherever cardiac catheterization is carried out to establish a well trained team of workers to ensure proper technic and adequate recording such a team usefully includes cardiologist roentgenologist cardiovascular surgeon and physiologic technician It is well to record the blood pressure in the superior vena cava in the right atrium in the right ventricle and in the pulmonary artery and its main branches by Hamilton manometer or by the newly introduced electromanometer (see Chapter 6) Samples of blood for determination of oxygen content are taken similarly from these various sources to determine if possible the entrance of oxygenated blood through atrial septal defect ventricular septal defect or patent ductus arteriosus (see Chap ter 13) The course of the specially modified ureteral catheter 100 to 125 cm in length can be followed fluoroscopically as it passes from one chamber to another or in abnormal hearts into left atrium or aorta and x ray films can occasionally be taken It is possible also to use such a catheter to explore

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Also Forssmann mentioned the fact that Christeller and Eisner had used Ung r s arterial method

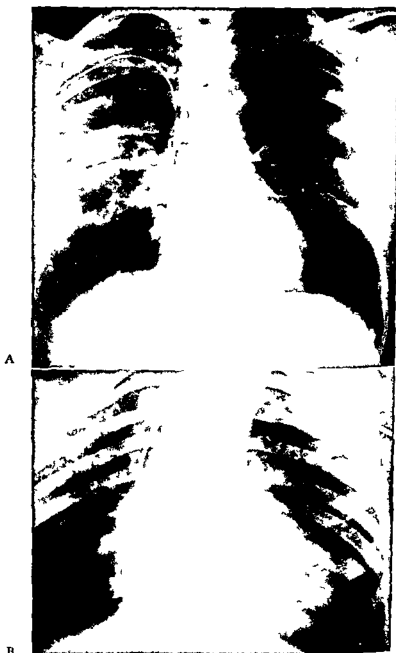
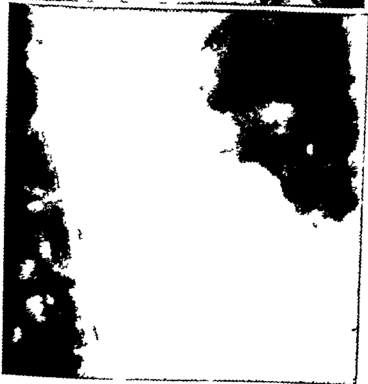


FIG 56 X ray films of thoraces with catheter in heart (*A*) Normal heart Cath
is seen entering the right atrium from the superior vena cava and its tip can be no
in the right pulmonary artery (*B*) Atrial septal defect with pulmonary stenosis
catheter is seen to pass from the right atrium through the septal defect to the left atr
and into a right pulmonary vein Note the lower position of the pulmonary vein
contrast to that of the artery



C



D

(*C*) Large patent ductus arteriosus The catheter is seen to pass from the main pulmonary artery through the ductus and down the descending aorta (*D*) Tetralogy of Fallot. The aortic arch is right-sided The catheter is seen entering the aorta from the right ventricle (Kindness of Drs Gordon S Myers, Massachusetts General Hospital Boston Bernard J Walsh Washington D C and Lewis Dexter Peter Bent Brigham Hospital Boston)

the coronary hepatic and renal veins and determine blood gases to study local organ metabolism Finally it is possible by the insertion of a special wire and electrode through the catheter to obtain right intra atrial and intraventricular electrocardiograms which as yet have been largely of academic interest (see Chapter 9)

In normal individuals the blood pressure in the superior vena cava has been found to be about 3 mm Hg in the right atrium 0 in the right ventricle 20 to 30 mm systolic and 0 diastolic and in the pulmonary artery 20 to 30 mm systolic and 5 to 10 mm diastolic With the catheter tip as far as possible in the pulmonary vessels an essentially capillary oxygen reading can be secured.

The oxygen content of blood samples taken from the superior vena cava and right atrium may vary considerably since the venous blood from various sources has not yet been well mixed For example a sample taken near the coronary sinus may have an oxygen content as low as 3 or 4 volumes per cent Mixing is more complete in the right ventricle ard pulmonary artery where the oxygen content usually measures between 10 and 14 volumes per cent

Under abnormal conditions with congenital septal defects and patent ductus arteriosus there are increased blood oxygen contents in the right atrium right ventricle and pulmonary artery according to the position of the left right shunt pulmonary vascular involvement and certain heart conditions may elevate the pressure readings even to levels as high as three or four times the normal

TESTS INVOLVING THE USE OF RADIOACTIVE ISOTOPES

Cutting across various special fields of internal medicine and applicable to a variety of tests in such fields has been the introduction of radioactive isotopes in the years that have followed World War II Even in therapy also this newly acquired knowledge has played a role, particularly in the form of irradiated iodine to reduce the activity of the abnormal thyroid gland in thyrotoxicosis or of the normal thyroid in combating intractable angina pectoris or congestive failure (a medical thyroidectomy) But radioactive isotopes have played a role much more prominently in diagnosis and re search than in therapy in cardiovascular disease In 1942 Hubbard et al used radioactive sodium to determine the velocity of blood flow in infants and young children This has been followed up since by Prinzmetal et al (1949) who have applied the method to adults In 1945 Nylin reported the determination of the circulating blood volume by the application of the new method worked out by Hevesy wherein blood corpuscles were tagged with radioactive phosphorus and the time of equilibrium of their dilution curves established by the use of the Geiger counter In normal cases the circulating blood corpuscles averaged 33 4 gm per kilogram of body weight while in heart failure there was a considerable increase with return to normal figures when the failure cleared in one case there was a drop of 28 per cent when congestion disappeared Using the same technic Nylin (1947 1948) has

studied the corpuscular and total blood volume in various organs including the lungs and the heart he found for example that 17 per cent of the total circulating blood volume was to be found in one lung and 13 6 per cent in the lower limbs Dow et al (1946) and Gibson et al (1946) used radioactive isotopes of iron similarly to measure the circulating red cell volume Prinzmetal et al (1947) studied the collateral circulation of the normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres and later (1949) used a specially constructed ink-writing Geiger Mueller counter to record the passage of radioactive blood through the heart chambers which they called radiocardiography Burch et al (1947) have used radioactive sodium to study congestive heart failure and Smith and Quimby (1947) Elkin et al (1948) and Wright et al (1948) have used radioactive sodium to study the peripheral circulation

EXAMINATION OF THE BLOOD

Blood examination affords a wealth of data concerning its various constituents and properties which are sometimes of much value in the study of a patient with cardiovascular disease

Hemoglobin Usually the hemoglobin in cardiac patients is within normal limits 80 to 90 per cent by various methods (13 to 15 gm per 100 cc of blood) Slight anemia down to 70 or even 60 per cent hemoglobin may occur in severe or long-continued acute rheumatic heart disease Moderate to severe anemia down to 55 or even 40 per cent hemoglobin is sometimes present in subacute bacterial endocarditis although slighter grades are more common The discovery of a low hemoglobin content due to hypochromic anemia of noncardiac origin or to primary pernicious anemia may prove helpful in explaining not only systolic but also diastolic heart murmurs due to cardiac dilatation resulting from the anemia Sometimes the differential diagnosis between anemia secondary to bacterial endocarditis and that secondary to other factors is difficult An abnormally high hemoglobin content over 100 per cent is found with polycythemia resulting from congenital heart defects which are attended by cyanosis and a right to left shunt of blood This percentage of hemoglobin may be as high as 150 (22 gm) or more Polycythemia vera may in turn be itself a factor of circulatory strain (see Chapter 23)

Recently an iron pigment in muscle called myoglobin which like hemoglobin has a function of picking up and storing oxygen has been under investigation (Biorck 1948) but further study is needed to ascertain the clinical significance of variations of its amount in heart muscle

Red blood cells The red blood corpuscles are decreased below the normal in number relatively less than is the hemoglobin in the anemia of acute rheumatic heart disease and in that of subacute bacterial endocarditis as in almost any secondary anemia They usually vary between 3 000 000 and 4 000 000 per cubic millimeter according to the severity of the anemia rarely falling to 2 500 000 or 2 000 000 or below in the severest grades of anemia found in

bacterial endocarditis In contrast in the morbus caeruleus of congenital heart disease the red cell count is as high as 6 000 000 to 12 000 000

White blood cells In infections of the heart the white blood corpuscle counts are increased A slight leukocytosis with a total count of 10 000 to 15 000 per cubic millimeter and a polymorphonuclear percentage of 70 to 85 is common in acute endocarditis rheumatic or otherwise although frequently in mild cases the number of white blood corpuscles is normal in the more severe and fulminating cases of bacterial endocarditis with complications such as embolic infarcts it can be much greater even to a total white count of 30 000 with 95 per cent polymorphonuclear cells Cardiac infarction from coronary thrombosis or embolism usually results in polymorphonuclear leukocytosis for a few days from a slight degree (12 000 with 75 per cent polymorphonuclear cells) to a high degree (25 000 with 90 per cent polymorphonuclear cells) depending on the size of the infarct A small infarct may result in no obvious leukocytosis

Sedimentation rate The rate at which the sediment of nonclotted blood settles out is much increased in many disease conditions including the infections involving the heart (rheumatism bacterial endocarditis and tuberculous pericarditis for example) and myocardial infarction from coronary thrombosis It is a useful test not in differential diagnosis but in helping to determine when an active process has completely subsided particularly subacute rheumatism infectious activity in a constrictive pericarditis and active tissue replacement in myocardial infarction It is important to correct the sedimentation rate index for marked variations in the cell volume percentage (hematocrit) of the blood for example a fast rate of 0 5 mm per minute (in a 100 mm sedimentation tube with heparinized blood) in a case with severe anemia may be corrected to a normal rate of 0 25 mm per minute found when the hematocrit is normal (at 45 per cent) (Rourke and Ernstene 1930)

Blood culture Bacteriologic examination of the blood is occasionally helpful in endocarditis The smear shows no organism but a culture when enough blood 5 to 20 cc is taken and the culture medium hormone broth with a hydrogen ion concentration of *p*H 7 6 is carefully prepared should reveal the presence of the Streptococcus viridans in the great majority of cases of subacute bacterial endocarditis Sometimes several cultures must be taken before positive ones are secured At least three or four positive cultures are essential for complete confirmation of the diagnosis of subacute bacterial endocarditis one or even two positive cultures may be more or less accidental findings Cultures are also useful in determining the particular organism streptococcus staphylococcus pneumococcus gonococcus or rarer bacteria responsible for acute bacterial endocarditis Infrequently in rheumatic endocarditis streptococci have been found in blood cultures and sometimes are thought to be responsible for the infection but blood cultures positive for streptococci have similarly been found in various other diseases and even in relatively normal controls especially when there are chronic foci of infection particularly dental and immediately after tooth extraction (not particularly

after tonsillectomy) This finding is best interpreted as indicating that occasionally stray bacteria may invade the blood stream without causing disease except in rare hearts where there may be suitable soil for their growth as in the case of subacute bacterial endocarditis

Serologic reactions Although on rare occasions such serologic tests as those for the gonococcus or the echinococcus may be helpful if carefully carried out it is only the Wassermann or allied (Kahn or Hinton) reaction for syphilis that is of routine value Because of the relative infrequency of cardiovascular syphilis in certain communities this reaction will prove negative in most cardiovascular patients in those communities but in other parts of the world where syphilis is rife and its treatment inadequate a positive Wassermann reaction will be commonly found When it is positive the test is of help in confirming a diagnosis of cardiovascular syphilis made on other grounds or in calling attention to its presence When negative this test for syphilis is of only limited value although the great majority of all patients with cardiovascular syphilis (about 85 per cent) yield positive Wassermann or Kahn or Hinton reactions Even when positive the reaction may be misleading for nonsyphilitic heart disease and incidental syphilis may be present in the same patient also other conditions like jaundice and subacute bacterial endocarditis may rarely yield slightly positive reactions These facts must be remembered and great care and judgment exercised before a positive Wassermann reaction is allowed to influence diagnosis prognosis and treatment there may be a justifiable suspicion of cardiovascular syphilis but symptoms or signs are essential to establish the diagnosis

Viscosity of the blood Viscosity of the blood chiefly dependent on its cellular content is rarely an important factor so far as the circulation is concerned and its measurement is largely a matter of academic interest Occasionally however its increase as in high grade polycythemia where it may be as much as three times the normal is a distinct burden for the circulation and a threat for thrombosis it has to be offset in part by capillary dilatation Decreased viscosity occurs in anemia and temporarily in congestive failure or with forcing of fluid intake

Chemical analyses Certain chemical analyses of the blood have become of routine value in internal medicine including cardiovascular disease An excess of nonprotein nitrogen beyond the normal upper limit of 40 mg per 100 cc of blood or of urea nitrogen beyond 20 mg per 100 cc means nitrogen retention which in turn means renal insufficiency but usually not primarily renal disease in cardiac patients congestion from heart failure may be the cause An abnormal increase is an accompaniment also of uremia which may act to poison the heart and of a renal shut-down due to dehydration The amount of blood sugar normally not over 120 mg per 100 cc of blood is worth knowing when diabetes mellitus is suspected because of the frequent association of this disease with early arteriosclerosis and because of its unfavorable effect on heart disease but too low a blood sugar (as from excess of insulin) may also act harmfully in acute coronary heart disease

The serum content of albumin and globulin in relation to cardiovascular disease has not been shown to be of clinical importance in the differentiation of cardiac edema from the edema due to liver disease or to malnutrition Any one of these factors may complicate the others In heart failure the serum protein is usually normal in the other two conditions much lowered (to 5 0 gm per 100 cc or less) especially in its albumin fraction Although it is possible to measure the contents of various ions in the serum (e g, sodium—normally 136–145 meq per liter potassium—3 5–5 0 meq per liter calcium—9 0–10 5 mg per 100 cc and chloride—100–106 meq per liter), much still remains to be learned about the significance of the blood content of salts and their elements acid and base along with the hydrogen ion concentration which remains strikingly constant (7 35 to 7 45) through buffer action Suggestions of the significant effect that may result from abnormality of such relationships is shown however in an unusual elevation of the *T* waves of the electrocardiogram in acidosis and in the case of a high potassium content (which may also induce or favor the occurrence of heart block—Thomson, 1939) and depression of the *T* waves in alkalosis and low blood potassium as well as in the case of hypocalcemia (in tetany) in which with very low blood calcium (4 to 5 mg per 100 cc of blood) the duration of systole as measured electrocardiographically is prolonged appreciably beyond the normal dropping again within normal limits when the blood calcium is restored to normal (10 mg) It is also important to remember that the serum content of salts does not indicate the intracellular chemical status Finally there are other substances for which on occasion the blood should be analyzed e g cholesterol in coronary heart disease and thyroid diseases especially (normally 150 to 250 mg per 100 cc serum) and vitamins in suspected avitaminosis (A normally 40 to 100 units per 100 cc C normally 0 4 to 1 0 mg per 100 cc)

Oxygen in the blood The normal content of oxygen in arterial and venous heart blood measured in terms of percentage saturation (if all the hemoglobin were oxygenated the saturation would be 100 per cent) is 95 per cent saturation (18–21 volumes per cent) for arterial blood and about 70 per cent saturation (10–16 volumes per cent) for venous heart blood For certain parts of the body the venous blood will show a greater degree of unsaturation but this excess is neutralized in the venous heart blood by a lesser degree of unsaturation in other parts of the body Stasis of varying degree and increased tissue metabolism account for the differences The more active the metabolism and the greater the stasis anywhere the less oxygen remains in the blood and the bluer it becomes The dissociation of oxyhemoglobin however requires a favorable temperature and if the air is very cold so that the skin is chilled the peripheral skin circulation although greatly slowed gives not a blue but a red color due to the presence of unreduced oxyhemoglobin

A helpful instrumental device called the oximeter (Millikan 1932) for the photoelectric determination of blood oxygen saturation in man by standardization against known blood samples can be applied to the ear or even to whole blood via cardiac catheter

A decrease in amount of oxygen saturation of arterial blood can be of degree it has been found to be as low as 58 per cent in a case of our of congenital heart disease with the tetralogy of Fallot and marked cya- (Talbott et al 1941) 32 per cent in a cyanotic and fatal case of the influenza epidemic of 1918–1919 (Stadie 1919) and even per cent in a case of bronchopneumonia with increase to 79 per cent through oxygen inhalation (Meakins and Davies 1925) A decrease in oxy gen saturation of arterial blood is due to any one of eight factors as listed herewith (1) Pulmonary congestion from heart (left ventricular) failure may be so great that in the distended pulmonary capillaries much venous blood passes through without contact with the alveolar wall and the oxygen on the other side of that wall also moisture in the alveoli may prevent the proper entrance of air (2) Pulmonary vascular engorgement from mitral stenosis without real heart failure acts in the same way (3) Pneumonic or other consolidation which causes a shunt of venous blood to the left heart through the capillaries of solid lung into which little or no air and oxygen can penetrate may also reduce the oxygen content of arterial blood (4) Destruction of a large amount over half of the total lung tissue may prevent sufficient air from reaching the pulmonary circulation (5) Chronic emphysema and asthma in which the respiratory exchange is very limited may also prevent sufficient oxygen from reaching the alveoli and blood stream (6) High altitudes 10 000 ft (about 3 000 meters) and over where the oxygen content of the inspired air is low do not allow a completely normal oxygen saturation of the blood At 14 200 ft elevation the oxygen saturation of the arterial blood has been found to vary between 80 and 90 per cent instead of the normal of 95 per cent or slightly more (Barcroft and associates 1922) and at 17 500 ft the variation was from 67 6 to 84 6 per cent (average 75 per cent) in six resident healthy workmen (Talbott and Dill 1936) (7) Poisoning by carbon monoxide or other toxic agert to cause methemoglobinemia may prevent some of the hemoglobin from taking up oxygen in the lung (8) Congenital heart disease may be attended by shunts that is through atrial or ventricular septal defects large enough to allow a considerable amount of venous blood to cross directly into the arterial circulation without first going through the lungs Congenital transposition of the aorta and pulmonary artery may also be a cause

Three additional observations about blood oxygen are of interest In anemia where the hemoglobin is low in amount its saturation with oxygen may be normal and yet the total amount available for the tissues too little With polycythemia as in congenital heart disease the saturation with oxygen may be abnormally low and yet the total content—volumes per cent—be sufficient because of the increased number of red corpuscles Also some oxygen can be carried directly in the blood plasma without attachment to hemoglobin this is not a large amount but it is of some importance the ratio of oxygen so carried to that combined with hemoglobin being about 1 to 50

An increase of oxygen saturation of normal arterial blood can be but slight since it already averages about 95 per cent saturated but when there is oxygen

unsaturation inhalation of air rich in oxygen (for example 50 per cent) may restore the blood saturation to normal

A decrease of oxygen saturation of venous blood below the normal arises first from the various factors already enumerated for decrease of oxygen in the arterial blood The tissues in removing their quota lower the percentage still more sometimes to a level close to zero in marked stasis Two important factors are added by the peripheral circulation itself (1) increased tissue metabolism from activity and (2) stasis of the circulation These may simply be local phenomena but if they involve enough of the body a very appreciable decrease of oxygen saturation of the venous blood in the right heart will result.

An increase of oxygen saturation of venous blood in the heart above the normal may be found (even up to 94 per cent) when there is a congenital left to right shunt from left atrium to right atrium or from left ventricle to right ventricle or from aorta to pulmonary artery (via patent ductus arteriosus) as determined by cardiac catheterization or when the circulation rate is very rapid and the metabolic activity of the tissues slight as in paroxysmal tachycardia or it may be found locally when there is rapid circulation which does not give time for the usual oxyhemoglobin dissociation or when there is an arteriovenous aneurysm (anastomosis)

Carbon dioxide in the blood The carbon dioxide content of arterial blood is normally about 60 volumes per cent i e 60 cc of CO gas per 100 cc of blood (26–28 meq per liter milliequivalents per liter = volumes per cent divided by 2 2) The carbon dioxide is carried in the blood chiefly in the form of the dissociated acid sodium salt whereby the carbon dioxide is quickly taken up and given off If an excess of other acids appears in the blood stream as sometimes happens in diabetes or nephritis the carbonic acid radical is decreased by the blowing off of more than the normal amount of carbon dioxide in the lungs to maintain the normal blood and body reaction Or there may be a retention of alkali from the blood to neutralize acid in the body tissue with corresponding decrease in the carbon dioxide content of the blood In alkalosis the carbon dioxide content of the blood is increased

A decrease increase or normal amount of carbon dioxide may be found in the arterial blood along with an abnormally low oxygen saturation of this arterial blood though at first thought only an increase might be expected. This variability of carbon dioxide content is dependent on the relative influence of three factors (1) reaction of the blood whether acidotic when in heart failure there is a retention of bicarbonate in the tissues producing a lowered blood carbon dioxide value or alkalotic due to excessive vomiting with elimination of acid gastric juice or to excessive intake of alkalies causing an increased carbon dioxide content in the blood (2) pulmonary overventilation due to oxygen want resulting in a decrease of arterial blood carbon dioxide doubtless a factor in keeping this content low in heart disease and pulmonary underventilation of extreme degree as in very extensive pulmonary disease resulting in excess of arterial blood CO and (3) a shunt of venous blood into the systemic circulation as in marked congenital heart disease

sufficient to transmit blood with a high CO content The product of all these factors determines the carbon dioxide content of the arterial blood There may be a rise of arterial CO to as high a content as 85 volumes per cent (in a case of extremely marked pulmonary disease—emphysema and purulent bronchiolitis of the left lung with right lung collapsed by hydrothorax—Meakins and Davies 1925) It may fall to as low as 30 volumes per cent or less from diabetic or uremic acidosis or even from the effect of high altitude (27 volumes per cent in a subject at 14 500 ft elevation—Barcroft and associates 1922) the normal content averaging about 50 volumes per cent In heart disease with congestive failure and decreased oxygen content of the arterial blood the carbon dioxide content of the arterial blood is more often decreased than normal or increased The test of alveolar air carbon dioxide has long been used in estimating the degree of acidosis in disease but it is not reliable in certain pulmonary conditions as for example when edema of the lungs is present

A decrease increase, or normal amount of carbon dioxide in the venous blood may be found as in the arterial blood but there are two additional variable factors (1) speed of blood flow from arteries to veins and (2) activity of tissue metabolism If the blood flow is fast or the tissue metabolism decreased less carbon dioxide is delivered to the blood in the capillaries and the difference between the arterial and venous carbon dioxide content may be reduced from a normal average of about 3 volumes per cent to 1 5 or even 1 per cent if the reverse occurs the difference may be increased up to 10 volumes per cent

Thus in judging the results of blood gas analysis many things have to be taken into consideration including accuracy of technic The data may pro[illegible] useful in helping to differentiate congenital heart disease with its shunts fr[illegible] acquired heart disease and in giving actual blood gas measurements for [illegible] degree of impairment of the circulation no matter what the cause The de[illegible]mination of the blood gases directly or by analysis of the alveolar air al[illegible] mits an estimation of the blood flow that is of the amount of blood p[illegible] by each ventricle per beat and per minute (see page 241)

Blood volume It is of some importance to distinguish between to[illegible] volume in any given person and circulating blood volume they [illegible] means synonymous It has been calculated that the circulating blo[illegible] in an adult of average size equals 5 to 5½ liters that is 3 liters [illegible] meter of body surface or 80 cc per kilogram of body weight (Go[illegible] al 1935) The mean plasma volume measured by Evans blu[illegible] amounts to 45 to 50 cc per kilogram of body weight (Cohen [illegible] 1948) the volume of the circulating red blood cells has been [illegible] use of radioactive phosphorus (Nylin 1945) and iron (Dow[illegible] Gibson et al 1946) and found to average 30 to 35 gm per kil[illegible] weight Various blood depots will on occasion quite sudden[illegible] considerable amount of blood from the active circulation to ho[illegible] for again by exercise or other requirement These normal blo[illegible] lungs and systemic veins (especially in the splanchnic regio[illegible]

spleen Abnormal blood depots are most commonly varicose veins of the legs, which may on occasion (chiefly with a change to the standing position) so drain the circulation of blood that faintness or even syncope may occur Other abnormal blood depots are varicose veins elsewhere than in the legs lax abdominal vessels and large hemangiomata These blood depots are over loaded in congestive heart failure and the actively circulating volume of blood is also too great not only for the strength of the heart but in actual amount as well (Gibson 1941) there may be a real hydremia In vascular shock the circulating volume of blood is on the contrary reduced (see Chapter 30)

Available fluid volumes of the human body can be measured by the dilu tion of sodium thiocyanate injected intravenously The subtraction of the plasma volume and 70 per cent of the red cell volume from the total of the available fluid volume gives the available interstitial fluid volume (Morse et al 1947)

EXAMINATION OF THE URINE

Quantity Most important in a patient known or believed to have a failing heart or constrictive pericarditis acute or chronic are the determination and interpretation of the quantity of urine excreted compared to the fluid intake This should be done not for twenty four hour periods but for twelve hour day and night periods for both fluid output and intake in order to note delay in excretion as well as limitation or excess of flow These measurements must be made with a reasonable degree of accuracy and fluid excreted by stool also calculated if the bowel movements are watery We must not forget however that normally a considerable loss of water occurs in the expired air and that the sweat glands of the skin excrete water Normally there should always be therefore an appreciably larger intake of fluid than output of urine in twenty four hours by a few ounces (100 to 200 cc) at least and by a much larger amount where there is much perspiration Knowledge of the amount of urine alone is of little value unless this amount is excessively increased or dimin ished

If the systemic venous pressure is raised to a high level for a considerable length of time because of congestive heart failure so that fluid which has *been distributed to the tissues at the arterial ends of the capillary* loops cannot be wholly reabsorbed at the venous ends the output of urine is decreased relative to the fluid intake and also delayed beyond the normal If the osmotic pressure in the capillaries is much decreased because of low serum protein as in nephrosis and malnutrition fluid leaves the circulation in too large an amount and the urine output decreases In either case a decreased urinary output is often a good warning of an impending edema With the beginning of diuresis the amount of urine increases and approaches and often surpasses the fluid intake and edema if present begins to subside It is well to keep a chart of these two measurements routinely day and night in the case of a cardiac patient with congestive failure of any grade at all

Specific gravity The specific gravity of the urine is of less moment than the quantity but usually varies with it When the urine output is much decreased in congestive heart failure the specific gravity tends to be high due to concentration (1 025 to 1 030) but in spite of a slight to moderate albuminuria it is not so high as with a like degree of oliguria in health when the function of normal uncongested kidneys permits full concentration (1 030 to 1 040 or more) When there is a large flow of urine with diuresis the specific gravity usually varies very little and tends to be low under 1 010 If there is poor renal function especially in chronic nephritis the night amount tends to exceed that of the day and the specific gravity usually maintains a fairly constant figure

The urine concentration test of renal function systematically introduced by Volhard (1918) but simplified by Fishberg (see his fourth edition of *Hypertension and Nephritis* Lea and Febiger Philadelphia 1939 page 77) is the most practicable of the various functional tests of the kidney for routine use Briefly it is as follows On the day and night of the test the subject drinks no fluid after the noon meal eating a dry supper The urine passed during the afternoon and at bedtime is discarded as well as any during the night The first urine passed in the morning is saved in a bottle After an hour more in bed a second specimen is passed into another bottle and still a third after being up and around for an hour without eating or drinking Fishberg writes

> The specific gravity of each of the three specimens is then taken If kidney function is unimpaired the specific gravity of at least one of the specimens will exceed 1 022 often going as high as 1 032 In very severe impairment of renal function the maximum specific gravity is but 1 010 and in intermediary cases figures between these extremes are obtained In every case exhibiting low specific gravity it is important to observe if edema is being evacuated for this may simulate inability to concentrate The third specimen passed while the patient is up and about occasionally helps in the detection of orthostatic albuminuria

Albumin Albuminuria is an almost constant finding in congestive heart failure the greater the congestion the more the albuminuria In the absence of any trace of edema its presence is far more significant of renal disease unless it is the slight inconstant so called orthostatic albuminuria or an accompaniment of infection In the case of subacute bacterial (Streptococcus viridans) endocarditis there is often important renal bleeding and damage albuminuria is therefore a frequent finding in this disease

Sugar Glycosuria may be transient slight and unimportant it may be of alimentary origin or the result of some accident like cerebral hemorrhage but usually it indicates diabetes mellitus mild or severe and then demands particularly conservative treatment in cardiovascular patients (see Chapter 23)

Urinary sediment Generally when there is congestive albuminuria red and white blood corpuscles and granular and cellular casts are found in the sediment of the urine With chronic nephritis hyaline casts are more frequent than in congestive heart failure With subacute bacterial endocarditis even though

there be no albuminuria red blood corpuscles are usually found in the sediment Gross blood in the urine is always important but is more likely to be due to local infection stone or malignancy than to heart disease Renal infarction secondary to emboli from a diseased heart in subacute bacterial endocarditis myocardial infarction with intracardiac thrombosis or mitral stenosis with atrial fibrillation is however an occasional cause of gross hematuria

Renal function tests The various tests of renal function simple or more elaborate may be applied in the presence of cardiovascular disease but their interpretation must be guarded The disturbance of renal function may be dependent on either renal disease or secondary congestion from heart failure The degree of renal impairment as indicated by most of the functional tests is dependent rather on the degree of involvement of the kidneys whether primary or secondary than on the type of involvement The combination of both primary and secondary involvement naturally results in the gravest disturbances of function One must wait until congestive failure subsides before making many deductions from renal function tests The most practical and useful tests are the urine concentration test such as that described above under Specific Gravity and the red (phenolsulfonphthalein) test in current use everywhere emphasizing however more the rapidity than the amount of the excretion it is more important to know what percentage of the dye is excreted in the first 15 minutes (normally 25 per cent or more) than in the total time of two hours (60 per cent or more)

CARDIAC OUTPUT MINUTE VOLUME OF BLOOD FLOW AND CIRCULATION RATE STUDIES PLETHYSMOGRAPHY

Cardiac output The cardiac output the minute volume of the blood flow and the speed of the circulation have been subjects for physiologic investigation for years chiefly in animals in the experimental laboratory During the last decade the application of such study to clinical medicine has been successfully begun

Long ago it was shown experimentally that the amount of blood pumped out by either ventricle in the course of a minute called the *minute volume of blood flow* could be determined readily by a formula (Fick 1870) based on the amount of oxygen taken up by the lungs in a minute s time and the amount utilized by the tissues This formula is as follows

$$\text{Minute volume of blood flow (in cubic centimeters)} = \frac{100 \times \text{cubic centimeters oxygen consumed in lungs per minute}}{\text{Difference in volumes per cent between oxygen content of arterial blood and that of venous blood}}$$

The application of this formula to man was for years fraught with difficulties though the discovery that analysis of the alveolar air permitted a close ap-

proximation to that of the blood gases of the right and left sides of the heart proved very helpful so that the minute volume of man could be ascertained and through that the stroke volume or output of each ventricle per beat (by dividing the minute volume by the pulse rate) Another method for determining blood flow was also used dependent on the absorption of certain gases from the lungs in a certain unit of time for example nitrous oxide acetylene and ethyl iodide acetylene proved to be the most suitable gas for this study (Grollman 1932) ethyl iodide giving figures 33 per cent too small

The introduction in recent years of cardiac catheterization has permitted a more accurate determination of the minute volume of blood flow by the use of the Fick formula since the oxygen content of the mixed venous blood in the right heart chambers can be readily measured and compared with the oxygen content of arterial blood This volume divided by the pulse rate gives the cardiac output per beat

Hamilton and his associates (1947 and 1948) have compared the Fick dye injection and pressure pulse curves in dog and man in relation to the cardiac stroke volume and have found a fair correlation between the dye injection and Fick findings and a close approximation between dye injection and pulse pressure contour

The application of heart volume changes between systole and diastole as determined roentgenologically has also been suggested recently (Hubacher and Nyffeler 1946) the difference in volume representing directly the stroke volume The difficulties inherent in measuring the heart volume by x ray however present a problem here that needs further development (see Chapter 7)

An ingenious but crude method of determining the output of the heart per beat and per minute was introduced by the use of the *ballistocardiograph* (Starr and Schroeder 1940 Cournand Ranges and Riley 1942) This instrument which consists of a delicately balanced table (on which the subject reclines) records the recoil of the body when the blood is ejected into the aorta and pulmonary artery from the ventricles Attempts have been made to correlate the graphic record which results called the ballistocardiogram (see Chapter 8) with the output of the heart as determined by the more direct methods noted above and can apparently with considerable corrections be used as a rough though inadequate gauge of the cardiac output the latest studies have indicated that the ballistocardiographic index was about one third too low Thus ballistocardiography is best used as a method of study per se and not to determine the cardiac output (see Chapter 8 and Figure 38 page 172)

The minute output at rest normally ranges from 3 500 to 9 000 cc (6 to 12 cc per 100 gm of body weight) being increased by exercise to as high as 25 liters or more in some cases It may like the stroke volume be reduced by various factors but usually to a less degree since an increase of pulse rate tends to compensate for a decreased output per beat The erect posture has been found usually to cause a decrease (even as much as 30 per cent or more

but usually less) of the minute volume calculated for the recumbent position Various other factors influence blood flow in a definite but sometimes indeterminable degree these are the stroke volume of the heart the lung capacity the absorption power of the lungs and the capillary diffusion areas of muscles Physical training makes these factors more favorable and so enables the circulation to be carried on more economically with less strain on heart and arteries as indicated by less elevation of pulse rate and blood pressure on exertion in the athlete than in the nonathlete Heart failure is usually attended by a decreased output but this is very variable and in some cases, as in thyrotoxicosis the output may still be elevated

It has been found that the normal output per beat or stroke volume varies in the average adult from 50 to 100 cc at rest but that in athletes it may be much higher, even 150 cc or more This is increased by exercise less in the nonathlete than in the athlete it may be more than doubled rising for example from 60 to 130 cc or from 70 to 150 cc on vigorous exercise With heart failure or extreme tachycardia it may be reduced in a case of paroxysmal tachycardia for example it has been reported to have dropped from 77 to 13 cc (Barcroft Bock and Roughton 1921)

Circulation rate In the past the volume of blood flow has been studied more than the rate but ingenious methods for determining the *rate of blood flow* through important parts of the circulatory system have been devised A pioneer method consisted of the injection of an active deposit of radium into the vein of one arm and the determination by means of a detector of the moment of its arrival in the heart and in the artery of the other arm (Blumgart and Yens 1927 Blumgart and Weiss 1927) The speed of flow from arm vein to heart and through heart and lungs to arm artery was thereby roughly determined Normally this arm to arm circulation time was found to vary from 14 to 24 seconds (average 18 seconds) a somewhat longer time than has been the finding in the case of more recently introduced substances injected this time increased with the pulse rate but not with blood pressure variations and was not affected by valvular disease The circulation rate was found to be decreased in congestive heart failure according to the degree of failure and also in atrial fibrillation without failure Arteriosclerosis and pulmonary emphysema did not cause a delay The arm vein to heart rate of travel of the radium injected blood showed a wide range of 2 to 14 seconds with an average of 7 seconds in normal individuals

The recent introduction of the employment of safe radioactive isotopes has revived this earliest method of determining the circulatory rate Hubbard et al (1942) tested the velocity of blood flow in infants and young children using radioactive sodium, Prinzmetal et al (1949) found the arm to right heart time to average 2 seconds normally in the adult with an additional 5 or 6 seconds to the left heart

Since the earlier days of the clinical application of the study of the rate of the circulation a decade or more ago numerous new methods consisting mostly of substances for injection into an arm vein have been introduced

These have included injections of a dye (brilliant vital red for example) fluorescein histamine (which flushes the face) sodium cyanide (causing a sharp increase in respiration) lobeline (causing a deep inspiration followed by a cough) Decholin (sodium dehydrocholate) (giving a bitter taste) glucose or saccharine (detected in the systemic circulation of the tongue by a characteristic taste) aminophyllin amyl nitrite (lung to face time as determined by a hot sensation) and calcium gluconate and magnesium sulfate (both causing a sensation of heat in pharynx and tongue) to test the rate of the blood flow from the venous side of the systemic circulation through the right heart lungs and left heart into the arterial side of the systemic circulation There is a wide range of sharpness of end point and of practicability among these various substances Hitzig (1947) and Blumgart and Altschule (personal communication) have preferred the use of Decholin with end point at 10 to 16 seconds which however has in rare cases caused allergic like reactions (Norman 1947) Baer (1940) found calcium gluconate the most desirable in 133 normal persons he found the arm vein to tongue time to range from 8 to 16 5 seconds averaging 12 3 seconds He injected 4 cc of 20 per cent calcium gluconate rapidly and then again in 2 or 3 minutes Papaverine HCl has also been suggested for determining the circulatory rate (Elek and Solarz 1942) 40 mg (1 25 cc) being the dose recommended an average of 20 8 seconds (15 4 to 27 0) has been reported between the time of injection and that of the end point a sudden deep inspiration In experimental animals acetylcholine has been tried with end point measured by direct inhibitory effect on sinoatrial node (Wilburne et al 1947)

To test the arm to lung time that is the integrity of the venous side of the systemic circulation and the right heart the injection of ether (Hitzig 1935) has been most practicable (using 5 minims of ether and 5 minims of normal saline) with end point detected by the subject s consciousness (or even the observer s note) of the presence of ether on the breath Baer (1940) found the ether arm to lung time in 169 normal individuals to vary from 3 to 9 seconds averaging 5 8 seconds Paraldehyde has also been introduced to test the arm to lung time (Caudel 1938)—the end point is shown by a cough in 100 adults with normal hearts the range was from 3 to 9 5 seconds averaging 6 seconds

Finally the inhalation of CO has been suggested to test the lung to brain time that is the integrity of the pulmonary circulation and left heart (Gubner Schnur and Crawford 1939) acting as a stimulant to the respiratory center its normal range has been found to be 5 to 10 seconds

Several investigators (Germandt and Nylin 1946 Meneely and Chestnut 1947 Nathanson and Elek 1947) have pointed out the delay in circulation rate that may occur as the result of dilatation of the heart alone even without congestive failure there remaining a certain amount of residual blood in the heart chambers immediately after their contraction

The tests of circulatory rate ordinarily employed are the ether time (normal average about 6 seconds) to determine the state of the right ventricle and

Decholin saccharine, or cyanide time (normal average 12 to 15 seconds) to test the total heart efficiency the subtraction of the former from the latter gives an estimate of the strength or failure of the left ventricle The tests are useful in a few cases in which there is some doubt especially in distinguishing in obscure cases between bronchial and cardiac asthma and in following given patients by serial tests but they are not routinely necessary

Plethysmography Plethysmography that is the measurement of volume changes of extremity or organ has been carried out chiefly in experimental animals but for certain purposes has been also applied to man It has been used to measure blood pressure to obtain fairly accurate records of the arterial pulse wave and especially to measure the volume of blood flow in a special part of the body It has little application to routine cardiovascular examination but in obscure or difficult cases of peripheral vascular disease it may yield information of value Of late a study of the electrical impedance of an extremity has indicated its possible use in the application of an electrically recording plethysmograph to investigations of the peripheral circulation (Nyboer 1950)

CALCULATION OF THE WORK OF THE HEART AND OF THE PULSE

Various attempts have been made to estimate the actual work of the heart and of the pulse some of these have proved of interest but they have not been of any practical value in cardiovascular examination We can for example express by a very rough formula the work of the left ventricle when we know the volume output per beat the heart rate and the mean arterial blood pressure If the left ventricle expels 100 cc of blood per beat at a rate of 60 beats per minute at a mean arterial pressure of 100 mm of mercury (about 1 300 mm of blood) it lifts 6 liters (6 000 cc) of blood to a height of 10 cm of mercury (or about 130 cm of its own weight) per minute which equals 780 000 gm-cm (or 7 8 kg meters) per minute The blood vessels maintain this volume at a somewhat lower level through diastole in addition to withstanding the systolic shock of the heart This rough calculation expresses in an interesting way the enormous constant activity of the heart It may further be applied to certain pathologic states for example if the mean arterial blood pressure is 150 mm of mercury and the heart rate 60 per minute and the output per beat 100 cc the work of the heart is 50 per cent greater than in the previous example given or 11 7 kg meters per minute Such a great increase in work if constant can explain the hypertrophy of the left ventricle found in hypertension

It has been calculated (Remington and Hamilton 1947) that the cardiac work performed in maintaining pressure is underestimated up to 12 per cent by multiplying the total ejection by the mean pressure during systole and that the work done by the heart in raising the pressure of the blood is 10 to 40 per cent more than that done at the periphery in forcing blood through the peripheral resistance energy to this amount being lost as the aortic wave is

More accurate formulas to include still other variables like velocity the effect of gravity and time intervals have been devised such as the following (Evans 1918)

Work of heart = $7\frac{Q \times R}{6} + \frac{W (V \times C)}{G \times E}$ where Q equals the quantity of blood ejected R equals the mean arterial resistance in meters of blood W equals the weight of the volume ejected V equals the mean velocity C equals the duration of the cardiac cycle G equals the acceleration due to gravity and E equals the period of systolic ejection The complication and incompleteness of such a formula however renders it impracticable except for experimental animals moreover it represents not the work of the whole heart but of the left ventricle alone The need of determining the output of the heart per beat by special methods the difficulty of ascertaining the mean arterial pressure the need of cardiac catheterization to estimate accurately the work of the right ventricle because for such calculation the pulmonary blood pressure must be measured in man and the apparent relative unimportance of the knowledge of the exact amount of work done by the heart have caused the general and probably justifiable neglect of such calculations as these in cardiovascular examination It is possible however that more attention paid to the actual work of the heart would be helpful at least in causing one to realize the great variability that exists not only in disease but also in health

Calculation of the work of the pulse as determined for example by sphygmobolometry (Sahli) or energometry (Christen) or otherwise has proved very complicated and of no practical value

FUNCTIONAL TESTS OF THE HEART AND OF THE CIRCULATION

Strength and endurance tests Both simple and complicated measures of strength and endurance have been proposed to gauge the health of the heart muscles and of the circulation as a whole These measures do demonstrate efficiency of the heart along with that of the muscles and nerves but it is frequently difficult to conclude to what degree abnormal limitation of strength and endurance is due to exhaustion how much to nervous fatigue and how much to myocardial weakness Dyspnea and angina pectoris are the two chief cardiac symptoms of overtaxation of the myocardium and when these symptoms are clearly singly and in a preponderant degree produced by tests of physical activity we may obtain valuable information about the heart When a sense of exhaustion in local muscles or generally throughout the body or when palpitation dizziness and faintness appear with or without dyspnea or heartache (not angina pectoris) other factors then enter in which prevent carrying the exertion far enough clearly to test the heart s rength this is the usual situation because of the general lack of physical training or because of the ready nervous fatigability in most individuals tested Hence these tests of strength and endurance generally amount to tests of training and of the nervous

state that is of physical fitness rather than of cardiac condition Neurocirculatory asthenia (or effort syndrome or soldier s heart) and muscular flabbiness are more easily and often exposed by exercise tests than is heart disease Nevertheless tests of strength and endurance may be applied with some success in estimating myocardial efficiency if sound judgment be shown in the interpretation of the findings

The simpler the test the better because a simple test is less likely to strain unaccustomed muscles less likely to exhaust prematurely a person not in good physical training and more convenient and practical to execute In fact such simple exertion as enters into the routine daily life of the patient is best of all. Questioning alone may suffice as to the production of dyspnea or of angina pectoris by climbing a flight or two of stairs at an ordinary rate of speed climbing a hill of moderate grade at moderate pace walking fairly rapidly on the level or lifting and carrying a handbag suitcase or heavy overcoat But if there is doubt or a need for exact data actual tests of these activities under the observation of the examiner should be executed Climbing a flight or two of stairs or if that seems too much pacing rapidly up and down the room or corridor or mounting and descending repeatedly an especially constructed two-step footstool are perhaps the best of the simple exercise tests A word of warning should however be added here namely that exercise testing in the case of serious coronary insufficiency can prove fatal

Under some circumstances as for example in examinations for military service athletic sport or other such activities more vigorous or special tests are suitable such as weight lifting hopping running and stepping repeatedly from floor to chair seat and back again Since however in routine civilian practice one deals often with older men and women or untrained persons with weak or undeveloped muscles these exercises are not usually applicable A trained athlete physically fit but with well marked aortic regurgitation may carry out vigorous exercise tests without any trouble while an untrained soft muscled man of the same age height and weight with a normal heart may be unable to complete relatively light exercise tests without much fatigue dyspnea and palpitation

The reaction of pulse rate and of blood pressure to exercise has been the subject of considerable study and discussion and has at times been thought to be a suitable test of circulatory efficiency, but the same remarks apply to this as to the production of symptoms Too marked a rise of pulse or blood pressure and too long a duration of this rise after rest begins go with poor physical condition as often as with cardiac weakness alone Normally after a short spell of exercise of moderate degree (like climbing rapidly two average flights of stairs or lifting during a time interval of one minute two five-pound dumbbells twenty times from the floor first to a standing position and then to an extended position of the arms above the head) the pulse rate and blood pressure in a well trained young or middle aged adult should return to normal from elevated levels within two minutes after lying down The more vigorous the exercise the more slowly do blood pressure and pulse rate return

to resting figures even in the normal subject The delayed rise of pressure is also of little or no significance normally there is a slight immediate fall when exercise begins before the rise develops

Over a period of many years various functional tests have been introduced under the names of their respective proposers but thereafter as a rule speedily forgotten Cabot and Bruce for example in 1907 described a group of such tests and imposed a modification of their own There has however been in routine use for quite some years especially in military circles a certain test for general physical and circulatory efficiency which despite its obvious im perfections has continued to be commonly employed This is the Schneider Index (1920) It is carried out as follows

1 The patient reclines for five minutes (a) The heart rate is then counted for twenty seconds When two consecutive twenty second counts are the same this is multiplied by 3 and recorded The score is noted according to Part A Table 1 (b) The systolic blood pressure is next taken by auscultation two or three readings are made as a check

2 (a) The patient stands at ease for one or two minutes to allow the pulse to assume a uniform rate When two consecutive twenty second counts are the same this is multiplied by 3 and recorded The score is obtained by the use of Part C Table 1 The difference between the standing and reclining pulse rate is scored then by use of Part B Table 1 (b) The standing systolic pressure is next taken The difference between this and the reclining systolic pressure is then scored by Part F Table 1

"3 The patient next steps on a chair about 18 inches high, five times in fifteen seconds timed by a watch To make this test uniform he stands with one foot on the chair at the count one this foot remains on the chair and is not brought to the floor again until after the count five At each count he brings the other foot on the chair and at the count down replaces it on the floor This should be timed accurately so that at the fifteen second mark both feet are on the floor (a) Imme diately while he stands at ease the pulse rate is counted for fifteen seconds this is multiplied by 4 and recorded (b) Counting is continued in fifteen second intervals for two minutes record being made of the counts at 60 90 and 120 seconds

The data from (a) will be scored by Part D Table 1 taking the difference between this exercise pulse rate and the standing rate The data in (b) are scored according to Part E Table 1

The total score is then added up in Parts A B C D E and F of Table 1 (see next page) The maximum possible is plus 18 and the minimum is minus 11 A score above plus 9 is considered normal a score of 9 or less fails to pass and is reason for a search as to the cause

A newer test of physical fitness for strenuous exertion superior in its appli cation to athletes and simpler in its execution than the Schneider Index was developed at the Harvard Fatigue Laboratory and is called the Fatigue Lab- oratory Index (Johnson Brouha and Darling 1942) It is carried out as follows The subject works at a standard hard exercise until he is exhausted

or if not exhausted for five minutes The pulse is counted in recovery from 1 to 1½ from 2 to 2½, and from 4 to 4½ minutes The score is calculated from the formula

$$\text{Index of fitness for hard work} = \frac{\text{Duration of exhausting work in seconds} \times 100}{2 \times \text{sum of pulses from 1–1½ 2–2½ and 4–4½ minutes after the end of work}}$$

The larger the score the better the subject 100 being a very good score Any form of exercise can be used provided it puts sufficient stress on the circulatory system by involving large muscle groups provided not more than two

Table 1

POINTS FOR GRADING CARDIOVASCULAR CHANGES IN SCHNEIDER'S TEST OF PHYSICAL FATIGUE AND EFFICIENCY

SCHNEIDER INDEX

A Reclining pulse rate		*B Pulse rate increase on standing (points)*				
Rate	*Points*	*0–10 Beats*	*11–18*	*19–26*	*27–34*	*35–4*
50– 60	3	3	3	2	1	0
61– 70	3	3	2	1	0	1
71– 80	2	3	2	0	−1	[illegible]
81– 90	1	2	1	−1	−2	−3
91–100	0	1	0	−2	−3	3
101–110	−1	0	−1	−3	−3	3

C Standing pulse rate		*D Pulse rate increase immediately after exercise*				
Rate	*Points*	*0–10 Beats*	*11–20*	*21–30*	*31–40*	*40 50*
60– 70	3	3	3	2	1	0
71– 80	3	3	2	1	0	0
81– 90	2	3	2	1	0	1
91–100	1	2	1	0	−1	−
101–110	1	1	0	−1	−2	−3
111–120	0	1	−1	−2	−3	3
121–130	0	0	−2	−3	−3	−3
131–140	−1	0	−3	−3	−3	−3

E Return of pulse rate to (standing) normal after exercise

Second	*Points*
0– 30	3
31– 60	2
61– 90	1
91–120	0
After 120 two to ten beats above normal	−1
After 120 eleven to thirty beats above normal	-

F Systolic pressure standing compared with reclining

Change in mm	*Points*
Rise of 8 or more	3
Rise of 2–7	2
No rise	1
Fall of 2–5	0
Fall of 6 or more	−1

thirds of the subjects can maintain it for five minutes and provided it does not demand some unusual skill for its successful performance The only equipment needed is a stopwatch and a means of administering a known amount of exercise at a constant rate Detailed instructions are given for using the test when a treadmill is available

Respiratory tests Most of the respiratory tests that have been employed to study circulatory efficiency are restricted in the same way in their clinical application as are the strength tests described above But here a further complication exists Diseases of the lungs pleurae or respiratory muscles can cause striking reductions in scoring just as can general weakness neurocirculatory asthenia and certain cardiac lesions

There are various respiratory tests the most practicable two being that of the vital capacity and that measuring the length of time that the breath can be held More complicated tests which measure symptom and pulse and blood pressure reactions to certain respiratory efforts such as maintaining an elevated air pressure in a closed system for a certain length of time or re breathing air in a closed chamber are open to the same objections as those already expressed concerning exercise tests they are tests of physical fitness more than of heart disease or failure also they are affected at times by the additional factor of possible pulmonary disease Although they may reveal myocardial insufficiency the degree of this must be very carefully interpreted and judged

Vital capacity The vital capacity of the lungs is the measurement by spirometer of the amount of air in liters that can be expelled by a complete forceful expiration after the fullest possible inspiration This test was first studied in considerable detail over a century ago (Hutchinson 1846) Normally the vital capacity varies with the size of the individual which is best calculated from the surface area the surface area can in turn be estimated roughly but accurately enough from the height and weight The normal ratio averages 2 5 liters of vital capacity per square meter of body surface A chart has been devised for the determination of surface area (Figure 28B page 143) and tables of average normal vital capacity for male and female American subjects have been constructed The vital capacity ranges normally from 3 to 4 liters for adult females and from 4 to 5 liters for adult males It varies somewhat with practice increasing as a rule on repeated tests until the subject becomes expert It varies also with physical fitness An athlete has a higher vital capacity than a nonathlete by as much as 25 per cent or more Furthermore the vital capacity is between 5 and 10 per cent higher in the erect than in the recumbent position In severely exhausted states and in marked neurocirculatory asthenia it may be much reduced even to 2 liters or less in an adult who is otherwise healthy with normal heart and lungs If inexperience exhaustion and lack of physical training are excluded as factors vital capacity reduction means infection thyrotoxicosis or pulmonary pleural mediastinal or cardiac disease

Vital capacity was originally studied to ascertain the degree of pulmonary

disease such as phthisis in which it is usually reduced Of primary cardiac conditions there are chiefly two that give rise to reductions of vital capacity mitral stenosis and congestive heart failure Pulmonary emphysema no matter what may produce it fundamentally is also an occasional cause of reduction of the vital capacity The greater the degree of any of these conditions cardiac or otherwise the lower is the vital capacity especially in the case of heart failure when there may be a reduction to below a liter such a high degree of reduction does not happen with uncomplicated mitral stenosis It has been reported that if there is pulmonary edema breathing dry air may increase the vital capacity as much as 10 per cent or more (Leas 1927)

The chief value of the vital capacity measurement in the study of a cardiac patient is in following the course of congestive failure A chart showing the vital capacity at intervals daily or every few days is of interest and sometimes of value in such cases but the test is a crude one and lags behind other evidence of change in the patient as often as it precedes it It may be concluded that the estimation of vital capacity in cardiovascular examination is not important as a routine measure except perhaps in pregnancy with heart disease when exertion is by order much restricted and reduction of the vital capacity may be the first indication of impending heart failure It is not delicate enough to demonstrate very slight grades of cardiac insufficiency and it does not give evidence of organic heart disease in the absence of failure except in the case of mitral stenosis which acts to decrease the alveolar air by causing engorgement of the lung vessels

Breath holding test A very simple respiratory test probably as useful as any other and because of its ease of execution the most practicable is the measurement of the length of time the breath can be held after a full inspiration All the qualifications with respect to the circulation made above concerning exercise and respiratory tests apply here also The breath holding test has one defect which applies only to certain cases and that is the possibility of malingering noted sometimes in soldiers during World War I it is possible however with experience to detect malingering Practice is sometimes important, as in the case of the vital capacity test A normal person in good physical and mental condition should be able to hold the breath for more than half a minute usually about three quarters of a minute and occasionally for over a full minute Extensive and expert training in underwater swimming and diving may enable an individual to hold his breath as long as two or three minutes or even a bit longer If the breath cannot be held as long as a half minute the test shows abnormality consisting of pulmonary or pleural disease congestive heart failure or lesser grade of cardiac insufficiency mitral stenosis general weakness or neurocirculatory asthenia

Anoxemia test The so-called anoxemia test was clinically introduced by Levy and his associates in 1939 to determine the functional capacity of the coronary circulation especially in persons suspected of having coronary heart disease but without clear-cut angina pectoris or electrocardiographic abnormalities The test is carried out as follows The subject breathes a mixture of

10 per cent oxygen and 90 per cent nitrogen for twenty minutes unless cardiac pain is experienced before the end of that time Electrocardiograms (preferably the precordial leads first) are taken routinely just before the test is started and at intervals of five minutes thereafter If the patient complains of discomfort a record is quickly taken the low oxygen mixture is shut off and 100 per cent oxygen administered for one minute

Two hundred and ninety three of these tests were carried out by Dr Levy and his associates 136 were done on persons apparently free of cardiac diseases and 157 were done on patients with coronary sclerosis Pain was not induced in any of the normal cases 74 or 47 per cent of the coronary cases complained of pain in 54 of which the pain came on during the first 10 minutes Positive electrocardiographic tests were observed in 77 or 49 per cent Positivity of the test was considered to be a total *RS ST* deviation greater than 2 5 mm Deviation was most marked in Lead 1 and in the precordial leads

The test has been found useful by Levy and his associates in doubtful cases but has not yet been widely adopted Some question of its safety has been raised and of the interpretation of slight electrocardiographic variations which might be within the range of normal (Burnett et al 1942) but in the hands of Levy and his associates (1941 and 1942) and of others since the test has apparently proved both useful and safe Careful clinical appraisal however makes rarely necessary either this anoxemia test or exercise tests though there are always a few individuals in whom the diagnosis may be difficult and for whom such tests are helpful if positive negative tests do not however rule out serious coronary heart disease with certainty

Tests of the peripheral circulation Numerous tests of the efficiency of the peripheral circulation have been introduced from time to time A decade ago a review (Montgomery Naide and Freeman 1941) summarized their diagnostic importance The tests have been divided into four groups (A) those which are a part of the physical examination and include observation of local tissue nutrition color and temperature of skin palpation of pulse and estimation of blood pressure in different limbs at various levels rate of blanching on elevation and of flushing and filling of veins on dependency and the reproduction of spasm by immersion of the extremity in cold water (B) tests of capacity of blood flow (vascular function tests) in skin as shown by vasodilatation by reflex heat artificial fever anesthesia (local general spinal and paravertebral) intradermal histamine and saline injections and reactive hyperemia (C) tests of capacity for blood flow (vascular function tests) in muscle by walking certain distances and by ergographic measurements of muscle fatigue and (D) test of past damage to arteries by oscillometry and roentgen ray studies especially by Diodrast injection of arteries or veins An additional method of study (E) has been more recently introduced consisting of the injection of radioactive isotopes especially sodium and following its course through any local circulatory area by Geiger counter (Elkin et al 1948) As in the case of judgment about the heart by tests so here too much

experience and common sense are needed for proper appraisal in many of the cases

BIBLIOGRAPHY

OTHER METHODS OF EXAMINATION

Cardiac Catheterization

Bing R J Vandam L D Gregoire F et al Catheterization of Coronary Sinus and Middle Cardiac Vein in Man *Proc Soc Exper Biol & Med* 1947 LXVI 239

Bradley S E Variations in Hepatic Blood Flow in Man During Health and Disease New England J Med 1949 CCXL 456

Burchell H B Parker R L Dry T J et al Cardiac Catheterization in Diagnosis of Various Cardiac Malformations and Diseases *Proc Staff Meet Mayo Clin* 1948 XXIII 481

Cournand A Baldwin J S and Himmelstein A *Cardiac Catheterization in Congenital Heart Disease* The Commonwealth Fund New York 1949

Cournand A and Ranges H A Catheterization of the Right Auricle in Man" *Proc Soc Exper Biol & Med* 1941 XLVI 462

Dexter L Venous Catheterization of Heart II Results Interpretations and Value *Radiology* 1947 XLVIII 451

Forssmann W Die Sondierung des rechten Herzens *Klin Wchnschr* 1929 VIII 2085

Landtman B "Mechanically Induced Disturbances in the Heart Action Observations Made on Heart Catheterization of One Hundred and Forty two Children *Acta paediatrica* 1950 XXXIX 1

Lenegre J and Maurice P La pression ventriculaire droite *Paris med* 1945 CXXIX 21

Limon Lason R Rubio Alvarez V and Bouchard F El cateterismo intracardiaco V Cateterizacion de las cavidades izquierdas en el hombre Registro simultaneo de presion y electrocardiograma intracavitarios *Arch del Inst de cardiol Mexico* 1950 XX 271

Sosman M C Venous Catheterization of the Heart I Indications Technics and Errors *Radiology* 1947 XLVIII 441

Soulie P Carlotti J Joly Fr and Sicot J R Catheterisme du sinus coronaire (Étude detaillée de 11 cas) *Arch d mal I coeur* 1949 XLII 818

van den Heuvel Heymans G Procaine amide (pronestyl) et arythmies cardiaques au cours du catheterisme du coeur *Acta cardiol* 1951 VI 53

Warren J V Stead E A Jr and Brannon E S Cardiac Output in Man Study of Some of Errors in Method of Right Heart Catheterization *Am J Physiol* 1946 CXLV 458

Zimmerman H A Scott R W and Becker N O Catheterization of the Left Heart in Man Circulation 1950 I 357

The Use of Radioactive Isotopes

Burch G Reaser P and Cronvich J Rates of Sodium Turnover in Normal Subjects and in Patients with Congestive Heart Failure *J Lab & Clin Med* 1947 XXXII 1169

Dow P Hahn P F and Hamilton W F "The Simultaneous Transport of T 1824 and Radio active Red Cells Through the Heart and Lungs *Am J Physiol* 1946 CXLVII 493

Flkin D C et al "The Study of Peripheral Vascular Disease with Radioactive Isotopes Part I *Surg Gynec & Obst* 1948 LXXXVII 1

Gibson J G 2nd et al "The Measurement of the Circulating Red Cell Volume by Means of Two Radioactive Isotopes of Iron *J Clin Investigation* 1946 XXV 616

Hubbard J P Preston W N and Ross R A 'The Velocity of Blood Flow in Infants and Young Children Determined by Radioactive Sodium" *J Clin Investigation* 1942 XXI 613

Meneely G R Wells E B and Hahn P F Application of Radioactive Red Cell Method for Determination of Blood Volume in Humans *Am J Physiol* 1947 CXLVIII 531
Nylin G Blood Volume Determinations with Radioactive Phosphorus *Brit Heart J* 1945 VII 81
Circulatory Blood Volume of Some Organs *Am Heart J* 1947 XXXIV 174
Nylin G and Hedlund S Further Studies of the Circulation with Radioactive Erythrocytes *Am Heart J* 1949 XXXVII 543
Prinzmetal M Corday E Spritzler R J and Flieg W Radiocardiography and Its Clinical Applications *J A M A* 1949 CXXXIX 617
Prinzmetal M Simkin B Bergman H C and Kruger H E Studies on the Coronary Circulation II The Collateral Circulation of the Normal Human Heart by Coronary Perfusion with Radioactive Erythrocytes and Glass Spheres *Am Heart J* 1947 XXXIII 420
Smith, B C and Quimby E H Use of Radioactive Sodium in Study of Peripheral Vascular Disease *Ann Surg* 1947 CXXV 360
Wright H P Osborne S B and Edmonds D G Rate of Flow of Venous Blood in Legs Measured with Radioactive Sodium *Lancet* 1948 II 767

Examination of the Blood and Urine (See also references under Blood Flow)

Barcroft J and associates "Observations upon the Effect of High Altitude on the Physiological Processes of the Human Body Carried out in the Peruvian Andes Chiefly at Cerro de Pasco *Phil Trans Roy Soc* London 1922 Series B CCXI 351
Biorck G "Myoglobin Its Properties and Occurrence in Man *Acta Cardiologica* 1948 III 223
Cohen J E and Shock N W Blood Volume Studies in Middle Aged and Elderly Males *Jour Gerontol* 1948 III 5
Erlanger J "Blood Volume and Its Regulation *Physiol Rev* 1921 I 177
Fishberg A M *Hypertension and Nephritis* Lea & Febiger Philadelphia 1939
Gibson J G 2nd 'The Clinical Significance of the Blood Volume *Ann Int Med* 1941 XIV 2014
Goldbloom, A A and Libin I with technical assistance of P K Roht Clinical Studies in Circulatory Adjustments I Clinical Evaluation of Studies of Circulating Blood Volume *Arch Int Med* 1935 LV 484
Groom D Wood E H Burchell H B and Parker R L "The Application of an Oximeter for Whole Blood to Diagnostic Cardiac Catheterization *Proc Staff Meet Mayo Clin* 1948 XXIII 601
Henderson L J Bock A V Field H Jr and Stoddard J L Blood as a Physicochemical System II *J Biol Chem* 1924 LIX 379
Henderson Y "The Volume of the Circulation and Its Regulation by the Venopressor Mechanism" *J A M A* 1931 XCVII 1265
Keith N M Rowntree L G and Geraghty J T A Method for the Determination of Plasma and Blood Volume *Arch Int Med* 1915 XVI 547
Lindhard J "A Dye Method for Determining the Blood Volume in Man" *Am J Physiol* 1926 LXXVII 669
Meakins J C and Davies H W *Respiratory Function in Disease* Oliver and Boyd Edinburgh and London 1925
Millikan C A "Oximeter Instrument for Measuring Continuously Oxygen Saturation of Arterial Blood in Man" *Rev of Scientific Instruments* 1932 XIII 434
Monge C et al *Estudios Fisiologicos sobre el hombre de los Andes* Facultad de Medicina, Lima 1928
Morse M Cassels D F and Schultz F W "Blood Volumes of Normal Children Available Interstitial Fluid" *Am J Physiol* 1947 CLI 438
Reith, A F and Squier T L "Blood Cultures of Apparently Healthy Persons" *J Infect Dis* 1932 LI 336
Rourke M D and Ernstene A C "A Method for Correcting the Erythrocyte Sedimentation Rate for Variations in the Cell Volume Percentage of Blood" *J Clin Investigation* 1930 VIII 545
Stadie W C "The Oxygen of the Arterial and Venous Blood in Pneumonia and Its Relation to Cyanosis" *J Exper Med* 1919 XXX 215

Talbott J H and Dill D B Clinical Observations at High Altitude Observatior Six Healthy Persons Living at 17 500 Feet and Report of One Case of Ch Mountain Sickness *Am J Med Sc* 1936 CXCII 626

Talbott J H et al A Record Case of the Tetralogy of Fallot with Comment Metabolic and Pathologic Studies" *Am Heart J* 1941 XXII 754

Thomson W A R The Effect of Potassium on the Heart in Man" *Brit Hea* 1939 I 269

Volhard In Mohr and Staehelin s *Handbuch der inneren Medi in* Berlin 1918

Wood E H and Geraci J E "Photoelectric Determination of Arterial O Saturation in Man *J Lab & Clin Med* 1949 XXXIV 387

Cardiac Output Blood Flow and Circulation Rate Studies Plethysmography

Baer S 'The Clinical Application of the Determination of Circulation Times *Int Med* 1940 XIII 2246

"The Measurement of the Velocity of Blood Flow" *Mod Concepts Card Dis* 1942 XI No 1

Baer S and Slipakoff B G 'The Measurement of Circulation Times and the A Used in Their Determination" *Am Heart J* 1938 XVI 29

Barcroft J Bock A V and Roughton F J Observations on the Circulation Respiration in a Case of Paroxysmal Tachycardia *Heart* 1921 IX 7

Bernstein M and Simkins S 'The Use of Magnesium Sulfate in the Measureme Circulation Time *Am Heart J* 1939 XVII 218

Blumgart H L and Weiss S "Studies on the Velocity of Blood Flow II III I VII VIII IX X XI The Velocity of Blood Flow in the Systemic and Pulmo Circulations in Health and Disease *J Clin Investigation* 1927 IV 15 149 173 399 and 555 1928 V 343 379 and 1928 VI 103

Blumgart H L and Yens O C Studies on the Velocity of Blood Flow I The Me Utilized" *J Clin Investigation* 1927 IV 1

Callebaut C Lequime J and Denolin "Détermination oxymétrique de la vitess culatoire chez l homme *Acta Cardiologica* 1950 V 137

Caudel S Determination of the Normal Circulation Time from the Antecubital to the Pulmonary Capillaries by a New Technic (using Paraldehyde) *Ann Int* 1938 XII 236

Cournand A Ranges H A and Riley R L "Comparison of the Results of Normal Ballistocardiogram and a Direct Fick Method in Measuring the Cardiac O in Man" *J Clin Investigation* 1942 XXI 287

Donzelot E et al Valeur de l épreuve a l éther pour le diagnostic de shunt arteriel Resultats dans 500 cas de cardiopathies congénitales *Arch d mal du c* 1949 XLII 601

Elek S R and Solarz, S D 'The Use of Papaverine as an Objective Measure of culation Time *Am Heart J* 1942 XXIV 821

Fick A "Ueber die Messung des Blutquantums in den Herzventrikeln *Sit ungsber der phys med Gesselsch zu Wur burg* 1870

Friedfeld L Marcus H R and Vorzimer J J "Aminophyllin Determination of culation Time" *New York State J Med* 1948 XLVIII 2047

Gernandt B and Nylin G "The Relation Between Circulation Time and the Am of the Residual Blood of the Heart *Am Heart J* 1946 XXXII 411

Gibbs F A Gibbs E L and Lennox W G "The Cerebral Blood Flow in Ma Influenced by Adrenalin Caffein Amyl Nitrite and Histamine" *Am Heart J* 1 X 916

Goodyer A V N Observations on the Impedance Plethysmograph *J Clin In gation* 1948 XXVII 536

Greenfield I Sodium Succinate as a Test of Circulatory Efficiency *Ann Int* 1950 XXXII 524

Grollman A *The Cardiac Output of Man in Health and Disease* Charles C Tho Publisher Springfield Ill 1932

Gross D "The Measurement of the Lung To-Face Time by Amyl Nitrite" *Am Hea* 1945 XXX 19

Gubner R Schnur S and Crawford J H "The Use of CO Inhalation as a Te Circulation Time" *J Clin Investigation* 1939 XVIII 395

Hamilton W F et al "Comparison of the Fick and Dye Injection Methods of Measuring the Cardiac Output in Man" *Am J Physiol* 1948 CLIII 309
Hamilton, W F and Remington J W Measurement of Stroke Volume from Pressure Pulse" *Am J Physiol* 1947 CXLVIII 14
Hitzig W M The Use of Ether in Measuring the Circulation Time from the Antecubital Veins to the Pulmonary Capillaries *Am Heart J* 1935 X 1080
"The Value of Circulation Times *Mod Concepts Cardiovas Dis* 1947 XVI No 8
Hubacher O and Nyffeler M "New Method for Determination of Beat Volume of Heart" *Cardiologia* 1946–47 XI 175
Hussey H H Cyr D P and Katz S The Comparative Value of Calcium Gluconate Magnesium Sulfate and Alpha Lobeline Hydrochloride as Agents for Measurements of the Arm to Tongue Circulation Time in 50 Patients with and 50 Patients without Heart Failure" *Ann Int Med* 1942 XVII 849
Krogh A and Lindhard J "Measurements of the Blood Flow Through the Lungs of Man *Skand Arch f Physiol* 1912 XXVII 100
Lysholm E Nylin G and Quarnå K "The Relation Between the Heart Volume and Stroke Volume Under Physiological and Pathological Conditions *Acta scand radiol* 1934 XV 237
M Michael J and Sharpey Schafer E P Cardiac Output in Man by a Direct Fick Method *Brit Heart J* 1944 VI 33
Meneely G R and Chesnut J L The Relation Between the Size of the Heart and the Velocity of the Blood *Am Heart J* 1947 XXXIII 175
Nathanson M H and Elek S R The Influence of Heart Size on the Circulation Time *Am Heart J* 1947 XXXIII 464
Newburgh L H and Means J H The Blood Flow in a Patient with Double Aortic and Double Mitral Disease (Pioneer study of blood flow in a patient) *J Pharmacol & Exper Therap* 1915 VII 441
Norman J K Reactions to Decholin in Circulation Time Determination *Am Heart J* 1947 XXXIV 740
Nyboer J Electrical Impedance Plethysmography A Physical and Physiologic Approach to Peripheral Vascular Study *Circulation* 1950 II 811
Ring G C Greisheimer E M Baier H N and others Electrokymography for Estimation of Heart Output Comparison with Direct Fick in Dogs *Am J Physiol* 1950 CLXI 231
Robb G P and Weiss S A Method for the Measurement of the Velocity of the Pulmonary and Peripheral Venous Blood Flow in Man *Am Heart J* 1933 VIII 650
Ross D N "Theophylline-ethylenediamine in the Measurement of Blood Circulation Time *Brit Heart J* 1951 XIII 56
Starr I and Schroeder H A Ballistocardiogram II Normal Standards Abnormalities Commonly Found in Diseases of the Heart and Circulation and Their Significance" *J Clin Investigation* 1940 XIX 437
Stead E A Jr and Warren J V "Cardiac Output in Man Analysis of Mechanisms Varying the Cardiac Output Based on Recent Clinical Studies *Arch Int Med* 1947 LXXX 237
Weiss S Robb G P and Blumgart H L 'The Velocity of Blood Flow in Health and Disease as Measured by the Effect of Histamine on the Minute Vessels *Am Heart J* 1929 IV 664
Werko L Lagerlof H Bucht H Wehle B and Holmgren A Comparison of the Fick and Hamilton Methods for the Determination of Cardiac Output in Man *Scand J Clin and Lab Investigation* 1949 I 109
Wexler J and Whittenberger J L Objective Method for Determining Circulation Time from Pulmonary to Systemic Capillaries by Use of Oximeter" *J Clin Investigation* 1946 XXV 447
Wilburne M Schlichter J G Grossman M and Cisneros F "Use of Acetylcholine in Objective Determination of Circulation Time and Fractionation of Vascular Bed Traversed" *Am J Physiol* 1947 CL 504
Winternitz M Deutsch J and Brull Z "Eine klinisch brauchbare Bestimmungsmethode der Blutumlaufszeit mittels Decholininjektion" *Med Klin* 1931 XXVII 986

Calculation of Work of the Heart and of the Pulse Sphygmobolometry Energometry

Barach J H "The Energy Index of the Circulatory System" *Am J M Sc* 1916, CLII 84
Christen T "Neue Wege in der Pulsdiagnostik" *Ztschr f klin Med* 1910 LXXI 39
Die dynamische Pulsuntersuchung F C W Vogel Leipzig 1914
Evans C L "The Velocity Factor in Cardiac Work" *J Physiol* 1918 LII 6
Remington J W and Hamilton W F Evaluation of Work of Heart *Am J Physiol* 1947 CL 292
Sahli H Die Sphygmobolometrie eine neue Untersuchungsmethode der Zirkulation *Deutsch med Wchnschr* 1907 XXXIII 628

Functional Tests

Biorck G and Pannier R One Hundred Positive Hypoxemia Tests" *Nord med* 1947 XXXIII 315
Brittingham H H and White P D Cardiac Functional Tests" *J A M A* 19– LXXIX 1901
Burnett C T Nims M G and Josephson C J The Induced Anoxemia Test *Am Heart J* 1942 XXIII 306
Cabot R C and Bruce H M "The Estimation of the Functional Power of the Cardiovascular Apparatus *Am J M Sc* 1907 CXXXIV 491
Hutchinson J On the Capacity of the Lungs and on the Respiratory Functions with a View of Establishing a Precise and Easy Method of Detecting Disease by the Spirometer" *Medico Chir Tr* London 1846 XXIX 137
Johnson R E Brouha L and Darling R C A Test for Physical Fitness for Strenuous Exertion" *Rev Canad d Biol* 1942 I 491
Leas R D Vital Capacity A Study of the Effect of Breathing Dry Air *Arch Int Med* 19 7 XXXIX 475
Levine S A "The Value of Determination of the Vital Capacity of the Lungs in the Care of Patients with Heart Disease *Arq brasil de cardiol* 1949 II 253
Levy R L Barach A L and Bruenn H G Effects of Induced Oxygen Want in Patients with Cardiac Pain *Am Heart J* 1938 XV 187
Levy R L Patterson J E Clark T W and Bruenn H G Anoxemia Test *J A M A* 1941 CXVII 2113 and *Am Heart J* 1942 XXIII 837
McClure C W and Peabody F W Relation of Vital Capacity of Lungs to Clinical Condition of Patients with Heart Disease *J A M A* 1917 LXIX 1954
Master A M "The Two-Step Test of Myocardial Function *Am Heart J* 1935 X 495
Montgomery H Naide M and Freeman N E "The Significance of Diagnostic Tests in the Study of Peripheral Vascular Disease *Am Heart J* 1941 XXI 780
Scherlis L Sandberg A A Wener J Dvorkin J and Master A M "The Effects of the Single and Double 'Two Step Exercise Tests upon the Electrocardiograms of 200 Normal Persons" *J Mt Sinai Hosp* 1950 XVII 242
Schneider E C A Cardiovascular Rating as a Measure of Physical Fatigue and Efficiency" *J A M A* 1920 LXXIV 1507

PART II

THE SIGNIFICANCE, PREVALENCE, CAUSES, AND TYPES OF HEART DISEASE

CHAPTER 11

THE SOCIAL AND ECONOMIC ASPECTS OF HEART DISEASE

Introduction The significance of heart disease is far reaching penetrating and affecting the health and happiness work and lives of all peoples on earth *and from* the cradle to the grave *Belatedly the medical profession has at long* last taken cognizance of this fact and has begun to enlist the support of patients social groups universities foundations and finally of local and national *governmental resources in the growing struggle to elucidate the* causes of heart disease and thereby to clear the way for their control

Heart disease or rather cardiovascular disease has become the chief public health problem of our day Ranking as the leading cause of death it has been widely but crudely publicized unwarranted fear of heart disease has swept the country in fact all the world Although it is true that the most recent and most accurate statistics do show a high incidence of cardiovascular deaths three very important considerations counterbalance in large part the seriousness of such a state of affairs In the first place cardiovascular disease or indeed heart disease itself is not just one disease but actually a multitude of different diseases most of which are quite unrelated except as they all involve the heart or blood vessels thus heart disease is very different from tuberculosis or typhoid fever or even cancer Secondly the increase in heart disease is in the older age groups there having been *actually a decrease in recent years* in heart disease mortality below the age of twenty five in the United States (Hedley 1939) An old person must die eventually of some disease process and a circulatory death *is as good to* suffer as any indeed probably better than many others Finally many grades of heart disease of various types are contrary to old time tradition mild and relatively unimportant compatible with considerable longevity and full activity

However despite these favorable points about heart disease it still leads other diseases as a cause of death from the age of five years to that of twenty it cripples many thousands of young people as the result of congenital defects and of rheumatic involvement of heart muscle and valves and it strikes down many leaders in professional business and political life in middle age at the

height of their careers of usefulness Thus there are many aspects of heart disease that concern society and national economy, in the home in the school in industry in the community and in the nation The present chapter has been newly added to this book in order briefly to discuss these special problems

Heart disease as it affects the home Heart disease presents many problems for the home which include the effects both of the chronicity of the condition and of the acute attacks that are so likely to punctuate its course Thus in children there are periods of rheumatic fever often very prolonged which require much patience of the family whether the youngster is in bed at home or away in a hospital or convalescent establishment Since many times in the absence of specific therapy these attacks last for months both child and parents become much depressed and need cheerful medical and nursing care It has been here that expert social service pioneering and recreational therapy when the state of health permits have played in late years an important role At the Massachusetts General Hospital Miss Edith Terry and Miss Lorena Love have established under the aegis of the Committee for the Home Care of Children with Heart Disease the In Bed Club with its badge and jacket and magazine home visiting schoolteachers and occupational therapy have added their share of aid for these children even before they graduate from bed to rejoin their comrades in the usual life of the community Not only are these patients followed in this encouraging manner while acutely and subacutely ill but they and their parents are seen at intervals thereafter to help them from acquiring the attitude so common in the past of resignation to lives of invalidism and fear Often the families need more instruction and building up of morale than do the children themselves And when much schooling is lost it has been found possible by easygoing and well controlled summer courses to promote the child to the class ahead along with his mates In Boston a good additional resource in the care of these children when subacutely ill has been the special foster homes of the Children s Mission when home care proved difficult and hospital attendance impossible or too prolonged

For the mother ill with heart disease acutely in childbearing age or older or chronically disabled the choice of an able and understanding housekeeper is not infrequently more important even than nursing care to relieve both mother and family of undue worry such a person can herself help with the actual nursing too unless the illness is very severe Another problem concerns the need in some cases of limitation of the size of the family and hence of some method or other of birth control expert advice is here often necessary since the risk of childbirth or even of a needed termination of pregnancy should not be countenanced

For the father ill with heart disease the threat of disability and death leaving the family not infrequently inadequately supported requires much careful planning with expert and friendly advice of doctor and business and professional associates It often in fact usually is not necessary for the man with heart disease to retire from his life work except perhaps for a few weeks or

months even after an acute coronary thrombosis Years ago it was common practice to advise retirement in such a case but fortunately we have learned better in the last twenty five years Moreover it is wise for a man young or middle aged immersed in his business or professional life to cultivate an avocation or hobby or two not too strenuous to which he may turn with pleasure if in later life he is prevented by illness cardiac or of other sort from continuing his business or professional life or indeed when he retires simply because of age

Finally there are the elders of the family grandparents and great grand parents who may have heart trouble the commonest ailment of the aged They may be a great burden for their juniors not only medically but socially and financially as well especially if they perforce reside with them Much better planning in the future will be needed than in the past to help solve this difficult problem especially since there will be constantly more and more old people in the world They themselves must plan better for their future when they are young their families must acquire a better attitude toward their elders with the respect for age that has been the Chinese tradition and finally the medical profession and the community itself must devote more time and interest to this problem of the care of old age which has been vari ously called gerontology and geriatrics a special field that will one day rank in interest and importance with pediatrics

Heart disease as it affects the school The youngest school children five and six years old may have heart disease either congenital or the beginning of rheumatic In fact these troubles may delay their entrance into school life by a year or more either because of the severity of the symptoms of the morbus caeruleus or because of active rheumatism which may be severe and prolonged at this early age and require months of bed rest Except for these two conditions however most children with heart disease at any age can safely and profitably attend school and need not in fact should not be separated off in special categories or classes except for rare individuals who are unusually crippled by early and marked valvular deformity cardiac arrhythmias or congenital defects of noncyanotic type It has not been found necessary to establish as at one time was planned special cardiac classes in the public schools Happily however in many communities home visiting is carried out by public and private schoolteachers when the children are well enough to receive them thus keeping up both instruction and morale And when the children do get back to school there is often a sensible arrangement whereby they may be watched and guided without making them overanxious resentful or set apart to do this there can wisely be a cooperative plan of schoolteachers parents and family doctor

The instruction itself in the upper classes in the teens can be skillfully directed toward an interest in sedentary occupations later in life if there is much heart trouble but often there is so little wrong (as for example slight mitral valve deformity or a small ventricular septal defect) that there need be no restrictions whatsoever present or future The same principles apply to

athletic sports and gymnastic exercises Infrequently it is necessary to curtail them but often it is wise to direct a child to baseball in preference to basket ball hockey or football and to short races and jumping in preference to marathon runs crew races, distance swims and heavy skiing

Most important of all in these various considerations is the individual himself No two patients are exactly alike and so it is vital to decide about every case on its own merits

Heart disease as it affects industry, business, and professional life In the past there has been much unnecessary fear of heart disease in its relationship to industry but happily a saner attitude is now developing as the result of informing the public at large of the accumulating experience of the medical profession During the last generation it has become quite evident in the first place, that the majority of persons with heart disease live a good many years after its onset in the second place that the great majority of such long survivors can live useful and contented lives and *finally* that they are with uncommon exceptions benefited rather than harmed by work to which they are accustomed for which they have been trained and which they enjoy Far too many cardiac invalids have resulted from the oversolicitous attitude of family friends or even physicians themselves and from the apprehension of industries businesses and professional associates and clients A recent survey of opinions of experts of the American Heart Association Committee of the Effect of Strain and Trauma on the Heart and Great Vessels has confirmed the experience of the author in this respect namely that the routin activity of persons in industry business and the professions if carried on in a sensible manner neither initiates heart disease nor makes it worse if it is already present unless it is very severe or going through an active stage as in the case of acute rheumatic carditis of acute or subacute coronary insufficiency or of myocardial insufficiency Under the conditions of such complications omission of work and rest at home or in hospital are of course indicated but often only temporarily for after these conditions have cleared up many persons can safely resume work to advantage to both morale and physical health to say nothing of their economic status in the support of themselves and of their families

One must of course separate off from the routine strains of industry business and the professions accidents and trauma physical or mental which can occur just as often at home or at play or in the crowded traffic of the present day (see Chapter 23) As a matter of fact acute coronary thrombosis and deaths from angina pectoris and cerebral vascular accidents are much more likely to occur away from work than on the job and often even in bed There should be a clearer understanding by industry and more widespread satisfactory insurance laws to meet the problem of the person with heart disease than have existed in the past One of the pioneers (Dr Irving Clark) in this regard who has had experience over many years in the employment of cardiacs in industry has emphasized the value and safety of so doing slowly this word is getting about Of course there must be safeguards

such as a careful appraisal of the individual at the beginning an examination annually or oftener if the need arises and proper treatment when complications come as they may whether the person is working or not Industry should not be blamed for such complications any more than some trivial accident which may have brought to light heart disease which has existed for years On occasion some unusual strain or trauma may expedite a complication and if so a justifiable and satisfactory attempt can be made to apportion the responsibility of such an exciting factor in the overall picture for example in a patient with a moderate or considerable degree of mitral stenosis some special strain may set off atrial fibrillation which might not have come on otherwise for some weeks or months or even a year or two but such strain should not be considered as 100 per cent responsible for the temporary disability that results it may not rate more than 10 per cent

These remarks apply to every kind of heart disease even the morbus caeruleus but of course youngsters with severe congenital or rheumatic heart disease should be trained in their youth for sedentary occupations and oldsters may need to reduce their time at work or sit instead of stand or shift to another job With regard to changing occupations one should add that a somewhat active job for which a person is trained at which he or she is skillful and which is well liked may afford actually far less strain than a new job which seems easier physically but which may prove both difficult and boring for the person concerned Thus one must individualize advice for every case lists of occupations for cardiacs may be somewhat useful bu they are only rough guides at best

We should not deprive our cardiac patients of education or some sort of occupation just because they seem hopelessly handicapped A good lesson in that respect was taught by a patient of mine with a high degree of the tetralogy of Fallot who because of much cyanosis and delicate health in early childhood received no schooling at the advice of the doctor in attendance because it was thought that such would be a waste of time and money However by good care and good luck he lived to be sixty years old but more important still by sheer will power and genius he educated himself to be one of the leading musical composers of his generation

Heart disease as it affects the community Much that has been discussed under the headings of home school industry business and the professions naturally applies to the community as a whole but there are other aspects of the community that deserve mention One is that of the general standard of living Where there is a low average level heart disease like a good many other diseases is more common It is well known for example that rheumatic heart disease is twice as common in the poorer more crowded sections of a city than in the suburbs where living conditions are better Much the same statement is true about cardiovascular syphilis only still more so Also the circulatory diseases of middle age both peripheral and cardiac are more subject to neglect under poorer conditions of living We do not as yet however have an adequate statistical appraisal of their varied incidence and it

may be that the overnutrition that is more likely to prevail among the well-to-do has its influence in the etiology or at least aggravation of the so-called degenerative diseases such as coronary atherosclerosis and hypertension A community sense of responsibility for health conditions builds up slowly but eventually leads to the establishment of a proper health agency in close harmony with private practitioners hospitals and medical schools Some small communities in the country today lack physicians close at hand they should join others in similar plight or perhaps better situated to set up some central group or hospital where someone trained in the field of cardiovascular disease can be available, as in other specialties with essential equipment such as electrocardiograph and fluoroscope

Heart disease as it affects the nation Next to last we come to the problem of the *national health That statistically* so far as the heart *is concerned* will be dealt with in the next chapter but there are a few additional comments to be made here In the first place heart and peripheral circulatory diseases are by far the most common causes of death in the U S A today and so naturally they hold the limelight in the current national health program Fortunately both public enterprise via the new National Heart Institute and National Advisory Heart Council established by act of Congress in 1948 and private enterprise headed by the American Heart Association organized in 1924 are working in close harmony in the support of research and teaching in the field of cardiovascular disease Happily research has the priority for it is evident that the sooner we discover and thereby learn to prevent the underlying causes of heart disease the sooner we shall rescue our young people and middle aged population from cardiac invalidism and death and the less effort time and money we shall need to plan for and expend in their care An increasing mortality from heart disease per se in the years to come need cause no alarm in fact such may be welcomed provided death comes quickly comfortably and quietly while at rest in bed or easy chair at an advanced age say at ninety after a long and happy and useful life But there is still tragedy in the newspaper headlines on occasion when some notable and public spirited citizen suddenly succumbs to heart disease in the very prime of life and at the top of his career

Heart disease internationally Finally the problem of heart disease is world wide and what has been said about its community and national relationships applies equally to all nations An International Cardiac Council was organized in Mexico City in 1946 to help to correlate the various national activities in the cardiovascular field and to aid in setting up the first International Cardiac Congress in Paris in the fall of 1950 At that congress there was established the International Society of Cardiology (Heart and Blood Vessels) There are herein many opportunities for future cooperative researches in the incidence and etiology of heart disease throughout the world and in the strengthening of international medical friendship

BIBLIOGRAPHY

SOCIAL AND ECONOMIC ASPECTS OF HEART DISEASE

Bellevue Hospital The Staff of the Work Classification Unit Adult Cardiac Clinic An Occupational Analysis of 580 Cardiac Clinic Patients *Circulation* 1951 III 289

Clark W I Jr Heart Disease in Industry *Boston Med and Surg J* 1922 CLXXXVII 21

Conner L A The Rehabilitation of Cardiac Patients Through Organized Effort *J A M A* 1927 LXXXIX 496

Cowdry E V *Problems of Ageing Biological and Medical Aspects* Williams & Wilkins Co Baltimore 2nd ed 1942

Dawber T R Meadors G F and Moore F E Jr Epidemiological Approaches to Heart Disease The Framingham Study *Am J Pub Health* 1951 XLI 279

Dolg n M Grossman M Simon A J Sorter H and Katz L N Cardiovascular Survey of Residents in a Custodial Institution for the Aged *J Gerontol* 1949 IV 39

Dublin L I "Heart Disease and Public Health *Am Heart J* 1942 XXIII 16

Public Hea th and Disease of Old Age (Summary) *Statistical Bull Metropolitan Life Ins Co* 1948 IX 1

Dublin L I and Lotka A J *Length of Life A Study of the Life Table* The Ronald Press Co New York 1936

Dunton W R and Licht S *Occupational Therapy Principles and Practice* Charles C Thomas Publi hers Springfield Ill 1950

Editorial The National Conference on Aging *J A M A* 1950 CXLIV 46

Emerson H Economic Aspects of Heart Disease *Am Heart J* 19_9 IV 251

Hedley O F Trends Geographical and Racial Distribution of Mortality from Heart Disease Among Persons 5–24 Years of Age in the United States During Recent Years (19?2–1936) *U S Pub Health Rep* 1939 LIV 2271

Kattwinkel E E Getting V A Morris E M Lombard H M and Robbins L C A Public Health Heart Program First Report *New England J Med* 1949 CCXLI 446

Kossmann C E Goldwater L J and de la Chapelle C E Selective Placement of Patients with Heart Disease in Competitive Employment *Am Heart J* 1947 XXXIII 700

National Heart Act. U S Public Law 655—80th Congress (Chapter 481— nd Session) (S _215) 1948

Probst E W "Employment of Hypertensives in Industry" *Indust Med & Surg* 1949 XVIII 462

Shepard W P The American Heart Association as a National Voluntary Public Health Agency" *Circulation* 1950 II 736

Sprague H B Mental Adjustments to Heart Disease The Factors Involved in Disability" *J A M A* 1939 CXII 2384

Ungerleider H E and Gubner R "Insurance Aspects of Heart Disease *M Clin North America* 1950 XXXIV 805

U.S Public Health Service New Clinical Center for Medical Research *J A M A* 1951 CXLVI 668

White P D The Problem of Heart Di ease in the Industrial Worker" *J Indust Hyg* 1921 III 219

Heart Disea e A World Problem *Bull New York Acad Med* 1940 XVI 431

"The Reversibility of Heart Disease *Illinois M J* 1944 LXXXVI 9

Wyckoff J "The Organization of the Cardiac Clinic *New York State J Med* 19_5 XXV 995

CHAPTER 12

PREVALENCE OF HEART DISEASE AND OF ITS ETIOLOGIC TYPES

The frequency of heart disease The first aspect of the prevalence of disease to be considered is that of its total frequency though actually is much less important than a second aspect to be considered later na that of the relative and absolute frequency of the various kinds of heart di dependent on the various causes Accurate information about either th cidence or the prevalence of heart disease in the community is as yet sca available anywhere in the world this information is obviously of grea portance and much work remains to be done in securing it We p scattered data of small or limited scope or of uncertain reliability fr number of sources data which are largely incomplete or otherwise unsat tory These sources include life insurance statistics periodic health sc industrial athletic and military examinations and hospital and mor figures

The estimation of community prevalence of heart disease has varied less than 1 per cent to several per cent The reported results of examin of school children have differed widely, but reasonably satisfactory stud the northeastern part of the United States have indicated that nearly 1 pe of children of school age have organic heart disease while in San Fran only 0 37 per cent of cardiacs were found among the school children half or more of whom had congenital heart disease (Sampson et al 1 and in Cincinnati the figure was midway 0 53 per cent with 55 per c them rheumatic and 45 per cent congenital (Rauh 1939) In 194 Robinson and his associates found among the San Francisco school chi 0 44 per cent of cardiacs which when further analyzed, showed 0 24 pe rheumatic heart disease and 0 19 per cent congenital heart disease How rheumatic heart disease was not at all rare among the children of California some ten to fifteen years ago as indicated by the finding of cent of cases at autopsy at the Children s Hospital in Los Angeles a patients through 14 years of age Eighty per cent of the cases at the Chil Hospital were California born (Thompson personal communication 1

At the Children s Hospital in Boston in 1949 1 3 per cent of the autopsied cases showed rheumatic heart disease and 10 per cent congenital (there were many infants)

The prevalence of heart disease in school children varies very much with climate because of the greater frequency of rheumatic heart disease in cold wet and high altitude areas for example Sampson et al (1945) reported 2 04 per cent rheumatic heart disease among the school children of Eureka in the extreme northern end of California in contrast to 0 32 per cent of rheumatic heart disease among the school children in Redlands in the extreme southern end of California The incidence of congenital heart disease was approximately the same in both places—0 07 per cent in Eureka and 0 08 per cent in Redlands In 1945 Wedum et al reported among school children in Denver 1 63 per cent with rheumatic heart disease

Among 28 139 young adults entering the University of Wisconsin between 1931 and 1939 there were 289 cases (1 + per cent) of heart disease with sex ratio of 1 7 females to 1 male (Cole 1941) From middle aged adult examinations and from the certainty that in old age the incidence of heart disease is very much higher than in youth it may be stated as probable that at least 2 per cent of the total population of the northern part of the United States have heart disease of a degree sufficient to produce symptoms or signs

As a cause of death heart disease has assumed greater and greater proportions in this part of the world until now it leads all other causes having far outstripped tuberculosis pneumonia and malignant disease the other three most common fatal diseases and also outnumbering accidental deaths which now rank in third place as a cause of death This increase which is absolute as well as relative is due to several reasons the individual importance of which is not yet known (1) more accurate cardiac diagnosis (2) fashions and revisions of recording diagnoses (for example coronary artery disease was classified some years ago under the heading of arterial disease in the Massachusetts state records while now it is classified under the heading of heart disease most persons formerly diagnosed as having Bright s disease are now recognized properly as having hypertensive heart disease with congestive failure and not primarily kidney disease and many persons who died of old age years ago would now be recorded as having died of cardiovascular disease) (3) reduction of incidence of certain other diseases especially of infections like infantile dysentery tuberculosis and typhoid fever with a corresponding increasing ratio of heart disease deaths and (4) actual increase of heart disease due in part at least to this very same decrease in mortality from other diseases Some individuals who in former days would have died of dysentery in infancy of diphtheria in childhood, or of tuberculosis or typhoid fever in early adult life now die of rheumatic syphilitic hypertensive or coronary heart disease instead See Table 2 and Figure 57 [1]

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[1] It is with much appreciation that I acknowledge the valuable assistance of Mr Felix E. Moore Jr., chief of the Biometrics Research Section of the National Heart Institute Bethesda Md in the revision of Table 2 and Figure 57 and for other helpful advice about this chapter

As a background for the increasing mortality from heart disease it is of interest to cite the decreasing death rate in the United States in 1900 the death rate from all causes in the registration states was 1,719 per 100 000 in 1910 it was 1 468, in 1920 it was 1 299, in 1930 it was 1 132 in 1940 it was 1 074 in 1945 it was 1 062 and in 1948 it was 988 The figures for Massachusetts are given in Table 4 It is of much interest that mortality from epidemics has been on the decline in late decades Except for the one serious

Table 2

MORTALITY STATISTICS FOR MASSACHUSETTS, 1900 TO 1945

(Cases allocated to place of residence since 1935)

Year	Death rate per 100 000 population				Total death rate per 1 000 population	Infant death rate per 1 000 live births
	Diseases of the Heart	Cancer	Tuberculosis (all forms)	Pneumonia (all forms)		
1900	165	75	214	172	18 4	*
1905	196	89	192	153	16 7	*
1910	200	94	164	175	16 1	*
1915	201	103	139	159	14 3	101
1920	215	115	114	156	13 8	91
1925	248	124	83	118	12 4	73
1930	282	136	64	93	11 6	60
1935	336	148	46	89	11 5	48
1940	412	169	38	58	11 8	38
1945	44[illegible]	187	39	49	1[illegible] 2	37

Source National Office of Vital Statistics

* Not available on comparable basis before 1915

epidemic of influenza at the end of World War I there have been no increases in mortality from epidemic disease since the beginning of the twentieth century (see Figure 58 for Baltimore)

In previous editions of this book it was stated that approximately one out of every three or four deaths in the U S A at large and in individual areas (such as the State of Massachusetts) was due to heart disease but steadily the proportion has risen so that now if we include all the ramifications of cardiovascular disease including for example renal vascular disease the ratio is very close to one out of two (49 5 per cent) Figure 59 illustrates well the recent data

The accuracy of death certificates is still subject to great improvement but it has gained rapidly during the last generation That the increasing percentage of cardiac deaths is not a unique feature of this country is shown by statistics recently received from France in Lyons from 1887 to 1891 deaths caused by heart disease made up 7 7 per cent of total deaths from known causes while from 1938 to 1940 they made up 17 3 per cent in large part apparently because of the reduction in mortality from other diseases since the actual number of cardiac deaths did not increase proportionately (Paris letter February 7, 1942 *J A M A* 1942 CXVIII 1155) This very increase in

mortality from heart disease provided it comes in old people may be a source for congratulation rather than dismay since it means that life is now being limited by the degenerative lesions of old age rather than by the infections of youth But such degenerative lesions should not appear in youth or middle age The relationship of morbidity and mortality to age is thus a vital one in any consideration of statistics of public health See Figures 60 and 61 on pages 271 and 272

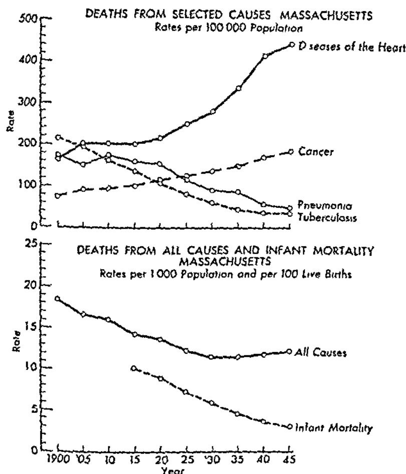


FIG 57 Death rates from diseases of the heart cancer tuberculosis and pneumonia and death rate from all causes and infant mortality rate Massachusetts 1900–1945

It is of great interest that the average duration of human life has more than doubled in the United States of America in the brief interval since its establishment 165 years ago It has been estimated that the average duration of life in this country in 1790 was about 30 years in 1930 it was 58 8 for white men and 62 4 for white women and in 1947 65 16 for white men and 70 54 for white women This greater longevity of females has been con

sistently 4 to 5 years for many decades (Dublin 1933 1941—*Statistical Bull Metropolitan Life Ins Co* 1949 XXX No 10) The expectation of duration of life among the Negroes in the United States in 1930 was 13 years less than that among the whites in 1947 it was reduced to 8 years In 1911 among the policyholders of the Metropolitan Life Insurance Company the expectation of life was 46 6 years and in 1949 less than four decades later it was 67 8 years In some parts of the world where infant mortality and youthful infections are still high the average duration of life is still only in the twenties about as it was probably in Europe in the Roman Era and in

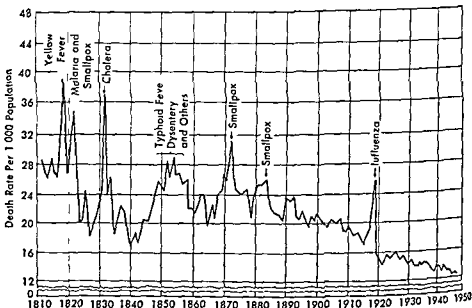


FIG 58 Annual death rates from all causes with indication of principal epidemics, Baltimore Maryland 1812–1948 (Kindness of the Metropolitan Life Insurance Company New York)

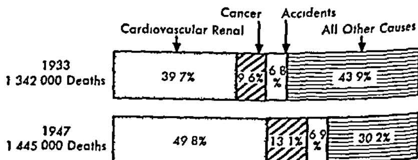


FIG 59 Proportionate mortality from leading causes of death in the United States of America 1933 and 1947 showing the increasing death rate from cardiovascular renal diseases (Kindness of Mr Felix E Moore Jr., National Heart Institute U.S Public Health Service Bethesda Md)

the Middle Ages (Figure 62) However despite the wonderful increase in the average duration of human life in this country in the past century or so the expectation of life for the man or woman who reaches 60 years is no greater now than it was years ago and probably a little less this is a very important aspect of the subject that should receive increasing attention in the future The longest lived persons (centenarians) are in the main those who with a good family inheritance of longevity have lived physically active lives in rural surroundings

Other relationships of morbidity and mortality from heart disease of great importance besides absolute and relative frequency and age are those to

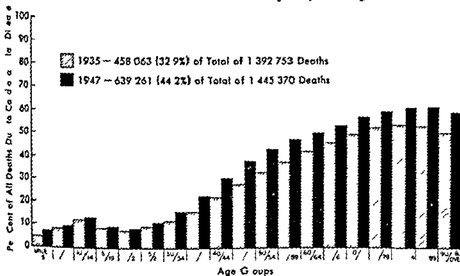


FIG 60 Chart showing total mortality from cardiovascular diseases as compared to all other causes according to age groups in the United States 1935 and 1947 (Kindness of Miss Marjorie Bellows American Heart Association New York City)

climate race heredity sex and social and financial status Favorable influences in reducing the incidence of heart disease in young as well as old are mild dry climates good but not rich food moderate physical exercise and healthful uncrowded living conditions Recently it has been noted that a good environment seems to be more important than having long lived parents in determining the individual s prospect for long life (*Statistical Bull Metropolitan Life Ins Co* February 1942 XXIII No 2) The importance of heredity in cardiovascular disease however is very great perhaps as great as or greater than any other factor but its exact significance remains obscure It has also been found that race is sometimes an important factor Negroes showing twice the prevalence of heart disease as do whites Sex is concerned in three respects in the first place there seems to be a law of nature throughout the entire animal kingdom from insects up to man that the male is considerably shorter lived than the female secondly sex affects the prognosis in every variety of heart disease males living usually a shorter time with any

given heart disease than females, probably in part because of the greater burden imposed by the more active life and thirdly it is related somewhat to the various etiologic types rheumatic heart disease and heart trouble from thyrotoxicosis being found more often in females and coronary heart disease and cardiovascular syphilis more often in males The whole problem of the incidence of heart disease needs however much further study

The causes of heart disease The second and the most important aspect of

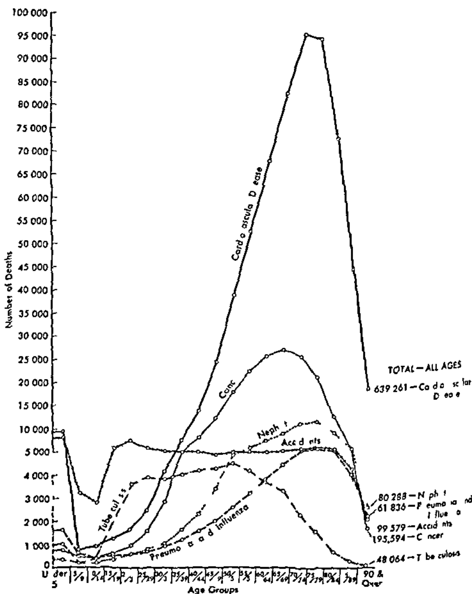


FIG 61 Chart showing total mortality from cardiovascular disease as compared to all other causes according to age groups in the United States 1947 (Kindness of Miss Marjorie Bellows American Heart Association New York City)

heart disease is that of its causes and their relative frequency With the developing interest in preventive medicine in recent years there has come the realization of the need of analyzing all disease from the etiologic standpoint Since heart disease is the source of much illness and of high mortality in nearly every community it has attracted much attention and efforts have been made to determine the relative and absolute importance of various factors thought responsible for heart symptoms and signs Preliminary classification of causes and etiologic types of heart disease has begun in several communities It holds much promise for the future for it is only as we see the importance of etiologic factors of disease that we can view them in due proportion and concentrate our efforts toward the eradication not only of the most

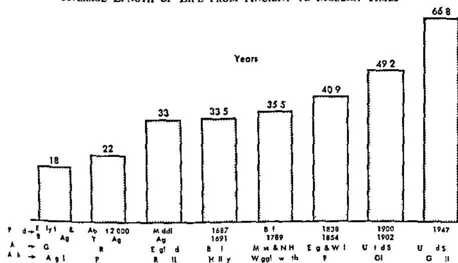


FIG 6? Chart showing the expectation of life from ancient to modern times (Kindness of Dr Louis I Dublin Metropolitan Life Insurance Company New York Published in *Length of Life* Ronald Press Company New York 1949)

serious pathologic states but also of those most amenable to such an attack in the current state of our knowledge

It is evident that although investigation of many causes of heart disease may well be carried on at the same time by workers all over the world the wisest course is to concentrate in any one community on that community s own particular causes most in need of control or most obviously open to attack In New England the rheumatic infection hypertension and presenile coronary disease are the most important factors now demanding study Many years will elapse before we are left with the problem of old age alone Meanwhile the practitioner of medicine may himself contribute to the progress either by concentrated study of some particular etiologic factor or factors or, in a routine way by recording as accurately and faithfully as possible in every patient with heart symptoms or signs the causes whether clear doubtful or

unknown Gradually in this way will come a better realization of the problems which lie before the medical profession in this large and important field

Lest it be thought that the effort of classifying each cardiac patient according to etiologic type is superfluous or an idle fancy of a public health Utopia I would hasten to add that for the individual patient himself the method is also of great value Accurate diagnosis prognosis and treatment may depend entirely on the recognition of the cause of trouble it can definitely be said that the etiologic diagnosis is often more important than that of either structural change or functional condition Congestive failure (myocardial insufficiency) and angina pectoris (coronary insufficiency) are of course of prime importance to recognize and treat as functional disorders but we can handle these cases much more intelligently if we know the fundamental cause of the disease back of their insufficiency For example congestive failure complicating coronary occlusion is more serious as a rule than that due to chronic mitral stenosis and angina pectoris in syphilitic aortitis is more significant than that in rheumatic aortic regurgitation in youth or in mild form in the coronary disease of old age

There are changing fashions in medical diagnosis A generation or two ago it was considered sufficient to ascertain the pathologic alterations present in the way of structural damage in the heart and textbooks were filled with a discussion of valvular lesions and myocarditis Then came a step forward when greater emphasis was placed on the functional state of the circulation than had been done before (Mackenzie 1908) This emphasis was much needed and served an important purpose but there has been a strong tendency as a result to make too light of the structural defects and indeed hardly to bother to look for them in detail The pendulum swung too far but there is now fortunately reappearing a growing respect for the lesions in the heart that can themselves serve as sources of strain and failure or that point to other disease processes or to other sources of strain in the body We must not think too little of either functional disorders or structural changes we must seek them all and make note of them at least those of most importance in cardiovascular diagnosis A functional disorder like paroxysmal tachycardia sometimes may be alarming but it is usually unimportant and far less significant in diagnosis than is mitral stenosis On the other hand a slight chronic rheumatic aortic regurgitation is far less important than is the serious functional disorder of angina pectoris

It is with the newest element of cardiac diagnosis the etiologic factor that this part of the book will deal This element has long been more or less recognized as of some importance but only in the last generation has it been emphasized properly (Cabot 1914) The following quotation represents a milestone in the progress of our study of cardiovascular disease

Cabot R C 'The Four Common Types of Heart Disease *J A M A* 1914 LXIII 1461

To classify cases of disease according to their pathogenic agent or process

and not solely by naming the region affected or the function disturbed is the ideal of scientific progress in medicine

"But until the last decade we have made little advance in this direction as regards the diseases which gravely disturb heart function Thus we still find in standard textbooks a section devoted to mitral regurgitation its diagnosis prognosis and treatment although mitral regurgitation is almost as vague a phrase as spinal paralysis or brain fever Just as a spinal paralysis may be due to trauma to the tubercle bacillus to the Spirochaeta pallida to the organism of poliomyelitis or to cancer so mitral regurgitation is only a symptom caused by the action of streptococci by the degenerative lesions of arteriosclerosis by the muscle tiring resistance of nephritic hypertension and probably by many other causes

"A similar criticism applies to all diagnoses of myocarditis The micro organism of rheumatism and of syphilis the ravages of arterial disease and perhaps many other causes may produce the lesions of chronic fibrous myocarditis with or without recognizable symptoms A diagnosis of myocarditis is like a diagnosis of ulcer it calls for an etiologic qualification such as syphilitic or tuberculous

'The matter has many practical aspects A sane prognosis and treatment of aortic regurgitation for example depends on knowing or guessing what disease has produced it Even physical diagnosis may have to await an intelligent interpretation of its results until we make up our minds what micro organism is at work in the heart as well as elsewhere in the body

While we should thus emphasize etiology and consider it first and generally foremost we must not lose sight meanwhile of the other two legs of the tripod of cardiac diagnosis structural change and functional condition All together the three elements complete satisfactorily our modern idea of analysis of a cardiac case Th represents another step in our progress and a sound one built upon the experience of the past and of the present Instead of diagnosing simply mitral stenosis or atrial fibrillation or rheumatic heart disease in a given case we should make the complete diagnosis of rheumatic heart disease (etiologic) with mitral stenosis (structural defect) and atrial fibrillation (disorder of function) (White and Myers 1921)

Heart disease may be very complicated Not only are there many different causes of trouble but two or more of these separate causes may occasion trouble simultaneously in the same heart and in different and even inconstant degrees Often much study and discernment are necessary to judge the relative responsibilities of several different causative factors in a given patient and in some cases it may be impossible to unravel the tangle In this volume the combinations of etiologic factors that are most common or important will be indicated in the discussion of complications in each chapter

In the present part of the book the more important causes and etiologic types of heart disease will be given by chapters chiefly according to age prevalence since that is a very practical arrangement leaving for later consideration certain factors of but slight or doubtful importance or of extreme rarity This plan seems better than that of arrangement according to importance or frequency because it leads one chronologically through the life history of man and because the various factors are of different prevalence and importance in

Table 3—THE RELATIVE PREVALENCE OF THE VARIOUS ETIOLOGIC TYPES

Etiologic Types of Heart Disease		USA (a a g d alphabet c lly)	ALABAMA R f h a d Porter 1948 2 418 cases 1 406 wh t 1 012 N Wh tes below N g al 1936 1946	CALIFO NIA (San Francisco) C ger 1 1936 3 535 ca es	COLORADO Da b 1939 701 ca es m ng 14 609 hospital dmi o s (4 8) in D er	ILLINOIS Fla man 1934 Cook County Hosp tal Ch cag 1 646 ases (1932 to 1933) bo e h vy l e Wh tes above e Ne ro es below Maher S iller nd Lill ii 1935 Ch go 1 000 c es below h avy l e	IOWA Myer 1927 Above li 510 c e out f t tal of 1 000 w th a dia symptoms r K s R th nd Paul 1933 B l w l ne 1 329 c ses U ers ty H t l I w City 1925 to 1931	LOUISIANA Holoubek, Holoubek d B ker 1947 8 313 a t p 1 Char ty H t l 1945 r rt d w e Wh t bo e N gro b l w	MINNESOTA Cl w 1941 4 628 a e m g 10 265 a t psies
Congenital anomalies			3.3† / 2.3	5.5†	1.7†	— / 0.0	2† / 2.0	1.3 / 9	—
Infection	Rheumatic type		11.5 / 14.5	22.2	24.8	19.0 / 10.4 / 24.2	36.0 / 2 3	4.74 / 6.3	18.6
	Subacute bacterial endocarditis		0.2 / 0.5	0.9	5.4	2.9 / 2.1 / 1.6	1.0 / 1.6	.86 / .6	11.0
	Acute bacterial endocarditis							.33 / .17	
	Cardiovascular syphilis		0.9 / 5.8	7..	2.6	8 / 27.1 / 9.5	5.0 / 6.2	2.55 / 15.6	7.0
	Oth s, i cl d g diphth t be culosi th viruses a d oth r f t tion							1.24 / .80	—
Thyrotoxicosis				2.9	0.5	3.0 / 1.6 / 9.3	1.5 / 8.7	— / .4	0.1
Hypertension	Systemic Hyperpiesis		55 / 62.4	21.5	30.4	53.6 / 60.4 / 26.2	24.5 / 34	12.35 / 28.15	55.5
	Pulmonary C pulm nal		0.9 / 0.7	0.9	0.9	2.1 / 0.2 / 3.8		— / .4	1.5
Coronary arteriosclerosis (including cases with angina pectoris)			5.8 / 5.7	33.6 n m [illegible] ted 24.9)	17.3	21.1 / 8.5 / 24.1	12.5 / 15.4†	12.3 / 6.4	25.9
Miscellaneous—T c states, tr um tum s, t			3.5 / 6.8		6.4	1.3 / 1.0 / —		1.0 / 1.0	—
Unknown			1.0 / 1.4			2.3 / 0 / —	4.5 / 2	— / .2	—

†Ex l d g those cases w th hype te si n

N w E N t ft t l t ymp b ed H k d Jone 1 28 2 421 se w h p 1 d bo h p rd d	Il h 1 t 1951 F t t mpl t d f 3 000 g 1 d botl u pl 0 3 te l d	N w Y C y pri t pat t) Wy k ff nd I gg 1926 1 001 s bo p se t bel	NEW Y K ST TE Phy ci) D P 1933 1934 ses (by 295	OHIO S II dse seam d G 1941 790 s R 6 548 a tops es Cl ln d C ty Ho p tal w t o d d f h art	OHIO (Cl 1 d) II e b a t ps es 49 2% diac ases lm & H ller les 1935 1940 80% 1948 2 000 co h t 20% Negro	OREGON C ff b low the l d as abo 1929 96 a d 1 344 pr the l e tops d ho r t l ate p t nt with rd c c ses ga ch t	PACI C N THWEST o g h td K g 1935 556 pri t pat nts w th	R KY MOUNTAIN t tal f 1 000 a th h a t t I k 1930 867 bl rg a ut f	Tr E FF th nd b lt pat t bo l L u 1913 645 ca e f Un rsty Hosp t N g oe below l e g Na h ll h t d White t	TEXAS St h t abo b y l ne s (whites a d I nza t 1927 C l e t l e 414 N g oes b l w S h b and S h lze 1931 d N groes)— mb l t ry b l w) 915 a es (501 bo 1 660 vy lin	VI INI p te pat W ts) d f ne d K mb 1 d g 112 N g oes gh 1926 300 ases (	WEST VIRGINI C d y 1932 118 c es	WASHINGTON D C 1 00 cas Hedl y 1935 gt n b Nb oe b G s (100 wh t B low h p t l in 1932 d D 1933 Abov h bo 6 e l vy l n 600 N g oe 450 f t l case 258 whit s abo e line vy l e b low) n W b 192
1 5%	7 9	0 7%	2 4%			0 1% / 0 %	0 9%	1 1%		1 0% / 0 2% / —	1%	0 8	— / 2 3% / 1 %
39 5 (4% hosp tal and 30 pri t)	23 5	45 8 / 25 5	27 2	15 1	12 0	13 / 11	20 0	44 0	15 3 / 4 3	10 4 / 3 6 / 4	22	3	2 / 4 7 / 1 1 / 8 3
1 9	1 2			3	13% among h m t	— / —		0 2		1 8 / 1 2 / —			1 8 / 1 0 / 5 4 / 3 6
Ra e	Ra	— 0 5	—	1		— / 2							
3 9	1 0	9 3 / 5 0	4 6	8 5		5 / 4	2 0	1 1	— / 15 4	9 2 / 31 6 / 12 7	11	1 6	4 3 / 15 5 / 5 0 / 21 3
Ra	R												
2 9	0 5	1 1		1 1		11 / 4	2 0	9 3		1 4 / 1 2 / —	31	5 9	3 / 1 2 / 0 8 / 2 1
29 2	26 2	1	20 1	33 4	27 6	70 / 38	49 4	14 9	65 1 71 8 combined	45 3 / 50 5 / 57 2	46	44 9	51 4 / 59 2 / 6 1 / 56 3
0 9	1 1	0 5		6 8					↑				↑
3 7	48 5	arterio-sclerot 18 4 / 43 5	8 8	22 4	51	17 / 21	20 3	21 1	↑	24 0 / 6 3 / 20 2	46	9 3	26 0 / 13 3 combined
2 1	1 7	t m 0 1		4	9 4	— / 3		0 9		1 4 / 1 2 / —			
3 4	0 6	19 5 / 8 1		2 4		— / — / 8	5 4	7 3		5 6 / 4 1 / —	2		

19 2 pe t f th pri t pat t h d g pe t n d only 93 pe nt of th hospital case

Table 3—Continued

Ft olog c Types of Heart Diseas		Hawaii B k d H twell 1949 81 949 med al dmuss ons 1 269 d c| at t	Puerto Ri o S s 1945 (1937 1944)	OTHER COUNTRIES (a ra ged alphabet c lly) Arg ntine Republic C 1943 10 000 a d ac pat e t (6 000 h [t] 4 000 pri te) B nos A res	Gon al S b th 1943 4 500 c ses (3 000 hospital 1 500 pri ate) K n	C l o-4 b ne 1943 3 594 ses (3 279 hosp tal 315 pri at) M d s	B azil (J) Cea 1948 438 ses	Rio J N o M I 1948 3 664 pat 1 I t of C d I gy 2 050 as I cases
C ngenit l n m lies		3.7	1.0	2.4	2.5	1.5	1.5	3.61
Infect	Rh mati type	17.3	17.4	18.2	18.4	25.0	9.3	9.3
	S b cut b t ri l ndoc d t	1.5			—			
	A ut b te al e doc dit s							
	C d ov cula yph li	2.2	6.1		9.0	6.8	14.3	15.5
	Oth l d g d phth ri t be los ru es a d oth nfestat	2.3						
Thy t cos		5.5	6	5.8	3.3	1.2	1.1	
Hype t n	Sy t mi Hype pies	32.2 Hype & C 8.8	22.8	23	20.0	23.0	45.2	23.5
	P lm ry Co pulm l	2.3		3.7	1.6	0.9		
Cor ry th oscleros (l di g ses th gi pe tori)		33	39.9	29.6	36.4	39.6	26.9	31.3
M scell eo —t t tes t ma l m rs t		1.7	10.2	8.9	8.8	2.0	1.3	16.8
U k		1.5				4		

By personal commu cati n t Cossi (1943)

S o P in Landul(I ial 1 4 t 21 pa ie mi ll 1 sa (be) 4 10[5] pa f yr 1 shes (be)		13.1/15.6		3.6/10.7		3.6/10.7	33.6/36.8	1.7/2.0	19.3/16.5	6.2/7.1	1.9/4.6
S o P o R m (nt (457 c) (al) 49 ( ) p t h f n (003) (b low)	0/1.0	21.0/1.55		18.2/2.6	0.4/—	1.1/1.2	23.7/67.6	5.5/1.3	17.3/5.5	2.4/1.2	7.0/0.8
Ces Cunева d the C l mbo C pat b l w l 1935 855 1 Hosp tal ab cl d g 4 5 f m nd 400 pri te	1[m]/—	20/8	2.1/—	10			13/25		21+/10+	many with se er an mia	
C lom ia Sal do-Sulg B ia 1947 3 2 p vat pat 1 n	2.1	8.4	0.9	7.2	—	3.0	36.1	3.6	25.0	33.5	
Costa Ric G C rella 1949 8 000 a t j Mo t l ty 9 6 a d o ase) r d sease	3.61	9.3		15.5	—	—	3.5	—	31.3	16.8	
E L n C md 19 6 1 000 pat nt Hosp tal es bo e l t l t pat ts bel w l e	2.0[m]/2.7	51.0/25.0	11/6	9.0/4.0	—	4.0/2.7	d o- (0 / 8.6		sev l 10.0/41.0		6.4/7.9
F NCE Leneg d Kil d 1949 3 P h sp t l pe l ng h rt lisea.	8	29.2		9.2			2r 8	5	32.4 (37.4 with combi n ti)	1	
I s l k 1940 10 104 medic l pati nt		38					41.3		20		
M x o ( ) er 1941 1,674 p t pati t bo h nt 726 h sp t l pat t bel w l	2.0/1.2	32.1/61.5	0.5	8.8/16.9		2.0	18.4/2.6		32.9/17.6	3.0/—	
N rw y Ormk g 1921 577 ase 58 m abo h 289 om n b low lin)		44.1/57.6		12.2/4.2							
South Africa H m and o oc les 1929 153 Eu o pe s (mostly Kaffirs)		41.8	9.1	5.5 (ma y a cu ry m)			some t m (? m- be)		16.3		
S AIN (M t h Ort l g 1949 19 0 1 000 c t ve (abu 1 000 pnea t a tops 2 l osp t l bel)	2/1.5	5.5/34.5	3	13.1/8	—/3.4	8.8	5/11.1	3.3/0	5.9/1.4	13.8/9.4	
A Ska d berg 1937 485 sa) rs 1 49 uht		21.3		11.7			41		18.0	4	

different parts of the world In New England for example rheumatic heart disease makes up an imposing percentage of all types put together and syphilis as a factor is relatively unimportant, while among the Negroes in the South rheumatic heart disease is far less common and cardiovascular syphilis far more frequent It is still too early to give satisfactory figures for the prevalence of etiologic types in different parts of the world only a few studies have been made which allow certain comparisons and these are not always parallel The surface has hardly been scratched A large amount of international cooperative research along these lines deserves early priority

I have tabulated on pages 276 to 279 the etiologic types of heart disease listed according to age incidence which may be found helpful as a guide to further study In this list will be found figures of percentage prevalence of the various types reported from New England New York Washington D C and several states of the South Middle West the Rockies and Far West in the United States and from England Norway South Africa Colombia Mexico the Argentine India, and the high seas The figures are often inadequate and of limited value but they are the best we possess today slowly they are increasing in number and accuracy (see Table 3 pages 276 to 279)

Finally we must at present leave a space in our classification entitled 'of unknown cause this is still an important group varying in different localities from about 1' or 2 per cent up to 15 or 20 per cent This very acknowledgment of our ignorance should act as a spur to us in our studies until eventually we may be able definitely to say we do know all the causes of heart disease With that knowledge there is bound to come more opportunity to prevent heart disease Incidentally there is an enormous miscellany of diseases which may depress the circulatory function or slightly or terminally alter the heart or the blood vessels (see the end of Chapter 23) but which do not deserve the designation of types of heart disease

To add important and useful information about heart disease in order to help fill the many and serious gaps in our knowledge has required the concentration of many workers in the past three or four decades especially since World War I (1914–1918) These men and women who have become specialists in this field have advanced our knowledge about cardiovascular disease further in that short interval of time than it had traveled in all the centuries that had gone before when few doctors had the interest or took the time to study the heart and circulation either in the normal man or in the cardiac patient This book which is largely a record of the work of the hundreds of students and investigators of cardiovascular disease since 1900 is a testament to that truth

BIBLIOGRAPHY

PREVALENCE OF HEART DISEASE AND OF THE ETIOLOGIC TYPES

Arenberg H Heart Disease Among Seamen *Am Heart J* 1937 XIII 197

Bainton J H Levy R L Munly W C and Pardee H E B (appointed by the Heart Committee of the New York Tuberculosis and Health Association Inc) *Criteria for the Classification and Diagnosis of Heart Disease* Paul B Hoeber Inc New York 4th ed 1943 (1st ed 1928)

Cabot R C 'The Four Common Types of Heart Disease An Analysis of Six Hundred Cases *J A M A* 1914 LXIII 1461

Case Records of the Massachusetts General Hospital Four Types of Heart Disease in One Case *New England J Med* 1941 CCXXIV 1108

Chavez, I 'The Incidence of Heart Disease in Mexico *Am Heart J* 1942 XXIV 88

Clawson B J 'The Incidence of Types of Heart Disease Among 30 265 Autopsies with Special Reference to Age and Sex *Am Heart J* 1941 XXII 607

Coffen T H "The Incidence of Heart Disease in the Pacific Northwest *Am Heart J* 1929 V 99

Cohn A E Statistical Studies Bearing on Problems in the Classification of Heart Diseases I Introduction *Am Heart J* 1926 I 442

An Analysis of the Apparent Increase in the Heart Diseases" *J A M A* 1935 CV 1394

Cole L R Cardiac Disease Among 28 139 Newly Entering Students at University of Wisconsin *Am J M Sc* 1941 CCI 197

Condry R J Heart Disease in West Virginia *West Virginia M J* 1932 XXVIII 485

Coombs C F 'The Aetiology of Cardiac Disease" *Bristol Med-Chir J* 1926 XLIII 1

Cossio P "Heart Disease in the Argentine *Am Heart J* 1943 XXV 145

DePorte J V Heart Disease in General Medical Practice Preliminary Report of Morbidity Survey Conducted by the New York State Department of Health *Am Heart J* 1933 VIII 476

Dublin L I Statistical Aspects of the Problem of Organic Heart Disease *Am Heart J* 1926 I 359

Dublin L I and Marks H H A Note on the Inheritance of Cardiovascular Disease—Result of Insurance Investigations *J Mt Sinai Hosp* 1942 VIII 482

Durbin E Heart Disease in Colorado *Rocky Mountain M J* 1939 XXVI 173

Emerson, H 'The Prevention of Heart Disease—a New Practical Problem The Shattuck Lecture *Boston M and S J* 1921 CLXXIV 587

Fishback H R An Analysis of Coroners Statistics from Cook County (Chicago) Illinois With a Pathologic Review of the Causes of Death *Arch Path* 1934 XVII 775

Flaxman N Heart Disease in the Middle West Incidence and Etiology of One Thousand Six Hundred and Forty six Cases at the Cook County Hospital *Am J M Sc* 1934 CLXXXVIII 639

Gager L T and Dunn W L "Heart Disease in Washington D C Study of Etiologic Types and Factors of Race Age and Sex in One Thousand Two Hundred Cases *M Ann District Columbia* 1933 II 112

Geiger J C Sampson J J Miller R C and Gray J P "A Survey of Heart Disease Morbidity in San Francisco *Am Heart J* 1936 XII 137

Goodman M and Prescott J W Heart Disease Among Adolescent School Children of New York City *J A M A* 1934 CIII 157

Grant R T After Histories for Ten Years of a Thousand Men Suffering from Heart Disease A Study in Prognosis *Heart* 1933 XVI 275

Gunewardene H O *Heart Disease in the Tropics* Butterworth and Co., Ltd Calcutta 1935

Hartwell A W and Lam J W "Heart Disease in Hawaii Review of 160 Consecutive Cardiac Cases seen in General Medical Clinic in Honolulu. *Hawaii M J* 1943 III 71

Hedley O F "Study of Four Hundred and Fifty Fatal Cases of Heart Disease Occurring in Washington (D C) Hospitals During 1932 with Especial Reference to Etiology Race and Sex" *U S Pub Health Rep* 1935 L 1127

Trends Geographical and Racial Distribution of Mortality from Heart Disease Among Persons 5-24 Years of Age in the United States During Recent Years (1922 1936) *Ibid* 1939 LIV 2271

Heimann H L Strachan A S and Heyman S C Cardiac Disease Among South African Non Europeans Preliminary Note *Brit M J* 1929 I 344

King R L Heart Disease in the Pacific Northwest An Analytical Study of Mortality and Morbidity with an Analysis of Five Hundred and Fifty six Private Cases *Northwest Med* 1935 XXIV 154

Laws C L "The Etiology of Heart Disease in Whites and Negroes in Tennessee *Am Heart J* 1933 VIII 608

Mackenzie J *Diseases of the Heart* Henry Frowde Hodder and Stoughton Oxford University Press 3rd ed 1913 (1st ed 1908)

Maher C C Sittler W W and Elliott R A Heart Disease in the Chicago Area A Study of the Etiological Factors in One Thousand Cases *J A M A* 1935 CV 763

Metropolitan Life Insurance Co How Stable Is Our Death Rate? *Statistical Bull* 1938 XIX 6

Myers M M The Symptoms of Heart Disease A General Discussion of Pain and Palpitation and a Report of a Study of 1000 Consecutive Patients *J Iowa State M Soc* 1927 XVII 388

Ormhaug T Om hjertesygdommenes aarsaker (Causes of Heart Disease) *Norsk mag f laegevid* 1921 LXXXII 868

Parson G W Analysis of 500 Cases of Organic Heart Disease Etiologic Types and Their Incidence" *Texas State J Med* 1941 XXXVII 518

Rathe H W and Paul W D Study of Incidence of Various Etiologic Types of Heart Disease in Iowa Review of One Thousand Thr e Hundred and Twenty Nine Cases *Iowa State J Med* 1933 XXIII 125

Rauh L W "The Incidence of Organic Heart Disease in School Children *Am Heart J* 1939 XVIII 705

Robey W H (representing New England Heart Association) "A Cardiac Survey of Children in Boston Public Schools *The Nation s Health* 1927 IX No 12 p 71

Rowntree L G McGill K H and Edwards T I "Causes of Rejection and the Incidence of Defects Among 18 and 19 Year Old Selective Service Registrants *J A M A* 1943 CXXIII 181

Salcedo Salgar J Clinical Analysis of 522 Private Cardiovascular Cases in Bogota Colombia *Proc Eighth Annual Pan American Scientific Congress* Washington D C May 16 1940 Dept State 1942 p 161

Sampson J J Christie A and Geiger J C Incidence and Type of Heart Disease in San Francisco School Children *Am Heart J* 1938 XV 661

Schwab E H and Schulze V E The Incidence of Heart Disease and of the Etiological Types in a Southern Dispensary *Am Heart J* 1931 VII 223

"Heart Disease in the American Negro of the South *Am Heart J* 1932 VII 710

Scott R W and Garvin C F Incidence of Types of Heart Disease Among 6 548 Autopsies with Observations on Race and Sex Presented before Am Heart A, Cleveland 1941

Stone C T and Vanzant F R Heart Disease as Seen in a Southern Clinic A Clinical and Pathological Survey *J A M A* 1927 LXXXIX 1473

Viko L E Heart Disease in the Rocky Mountain Region *Am Heart J* 1930 VI 264

White P D and Jones T D "Heart Disease and Disorders in New England" *Am Heart J* 1928 III 302

White P D and Myers M M "The Classification of Cardiac Diagnosis" *J A M A* 1921 LXXVII 1414

Whitney J S *Heart Disease Mortality Statistics* (U S Registration Area) Am Heart A New York 1927

Wood J E Jr Jones T D and Kimbrough R D The Etiology of Heart Disease Clinical Study of 623 Cases with Certain Observations on Race and Climate" *Am J M Sc* 1926 CLXXII 185

Wyckoff J and Lingg C "II Etiology in Organic Heart Disease" *Am Heart J* 1926 I 446

Recent References (1944–1950)

Berk M E and Hartwell A S Five Years of Heart Disease in Hawaii *Hawaii M J* 1949 VIII 177
Biorck G and Blomquist N "Studier over hjartkarlsjukdomarnas samhalleliga betydelse i Sverige Den svenska befolkningens dodlighet i cardiovasculara sjukdomar under åren 1911–1945" *Social Med Tidskrift* Stockholm 1949 XXVI 215 and 243
Collins S D Statistical Studies of Heart Disease V Illness from Heart and Other Cardiovascular renal Diseases in General Morbidity Surveys of Families *Pub Health Rep* 1949 LXIV 1439
Dublin, L. I Metropolitan Life Insurance Company *Statistical Bull* 1949 XXX No 10 1950 XXXI No 1 and No 3
Fenn, G K Kerr W J Levy R L Stroud W D and White P D "Re-examination of 4 994 Men Rejected for General Military Service Because of the Diagnosis of Cardiovascular Defects" *Am Heart J* 1944 XXVII 435
Gage R P Statistics and Medicine The Need for Close Cooperation Between the Physician and Statistician in Medical Statistics" *Proc Staff Meet Mayo Clin* 1946 XXI 130
Garcia Carrillo E "Some Cardiological Problems of the Tropics" *Am J M Sc* 1949 CCXVII 619
Gover M Statistical Studies of Heart Diseases III Heart Disease Associated with Other Major Causes of Death as Primary or Contributory Cause *U S Pub Health Rep* 1949 LXIV 104
IV Mortality from Heart Disease (All Forms) Related to Geographic Section and Size of City" *Ibid* 1949 LXIV 439
Gover M and Pennell M Y Statistical Studies of Heart Disease *U S Pub Health Rep* 1950 LXV 819
Hamilton B E Report from the Cardiac Clinic of the Boston Lying In Hospital for the First Twenty five Years" *Am Heart J* 1947 XXXIII 663
Holoubek J E Holoubek A B and Baker D T Heart Disease in Charity Hospital of Louisiana in New Orleans A Survey of 8 313 Routine Autopsies *New Orleans M & S J* 1947 XCIX 431
Juca A Causas Das Cardiopatias No Ceara *Med Cirurgia Farmacia* 1948 CLI
Landulfo J LeVoci I D Mascarenhas A and Spanghero C "Frequencia etiológica de cardiopatias na Cidade de Sao Paulo Revisao de estatisticas anteriores e estudo atual correlato na classe dos comerciarios *Arq brasil de cardiol* 1949 II 297
Lenègre J and Kalaidonis P Étude statistique de 500 autopsies de sujets morts d une hypertension arterielle ou d un affection cardiaque dans des services hospitaliers parisiens" *Sem d Hop de Paris* 1949 XXV 3115
Metropolitan Life Insurance Company "A Century of Progress in Longevity *Statistical Bull* 1949 XXX No 10
Health and Longevity at the Mid Century" *Ibid* 1950 XXXI No 1
International Variation in Longevity *Ibid* 1950 XXXI No 3
Moritz A R. Unexpected Death of Apparently Healthy Adults from Natural Causes *Northwest Med* 1948 XLVII 500
Murgel L Contribuicao estatistica a etiologia das cardiopatias no Rio de Janeiro *Bol M dico Cirurgico* 1948 X, 163
Ortiz Vazquez J "Incidencia de los diversos tipos de cardiopatias entre tres mil autopsias hospitalarias consecutivas *Revista Española de Cardiol* 1950 IV 166
Ortiz Vázquez J Duque A Perez Gonzalez P and Calderon Montero J Etiologia de las cardiopatias en Madrid Un analisis de mil casos consecutivos" *Revista Espanola de Cardiol* 1949 III 331
Porter R R "Cardiovascular Experiences in an Army General Hospital" *Am Heart J* 1944 XXVII 559
Ramos J Le Vocci I Ratto O Gorges S and Lindenberg S Frequencia etiologica das cardiopatias em Sao Paulo (Brasil)" *Arq brasil de cardiol* 1949 II 181
Robinson S J Aggeler D M and Daniloff G T Heart Disease in San Francisco

School Children 1947 Registry Showing Incidence Problems and Supervision Techniques *J Pediat* 1948 XXXIII 49

Suárez R M 'The Incidence of Heart Disease in Puerto Rico *Am Heart J* 1945 XXIX 339

Tecce N and Lombardi A Sulla reale incidenza delle malattie cardiovascolari tra le cause di morte *La Riforma Medica* 1949 LXIII 833

Tranchesi B Cavalheiro Dias J Nussenzveig I Tisi O G Tranchesi J and Fabio Lion M A etiologia das cardiopatias em Sao Paulo (Brasil) *Arq brasil de cardiol* 1951 IV 31

Traum A H and Wilcox B B Cardiovascular Disease Among Veterans of World War II *New England J Med* 1946 CCXXXIV 82

Vakil R J A Study of Rheumatic Heart Disease in Bombay Province (India) (From a total medical in patient population of 30 104 patients) *Indian Heart J* 1949 I, 15

Wartman W B and Hellerstein H K The Incidence of Heart Disease in ,000 Consecutive Autopsies *Ann Int Med* 1948 XXVIII 41

Welch O and Porter C Heart Disease in Alabama *Alabama State M A J* 1948 XVII 213

Woolsey T D and Moriyama I M Statistical Studies of Heart Diseases II Factors in Trends of Heart Disease Mortality *Pub Health Rep* 1948 LXIII 1?47

CHAPTER 13

CONGENITAL CARDIOVASCULAR DEFECTS

Introduction Congenital defects of the heart and blood vessels though not frequent comprise one of the most difficult important and interesting medical problems of our day More progress has been made in our understanding of their clinical significance and in their recognition during the last two decades than in any other type of heart disease the successive editions of this book which were begun just twenty years ago illustrate this well Also considerable and spectacular advances have been made in the surgical correction and amelioration of several of these defects and intracardiac catheterization has been applied especially in this field Table 5 (page 294) presents in summary th current clinical status of the congenital defects of the heart and great vessels Less important extremely rare or as yet undiagnosable defects are not included in this table but are for the most part mentioned in the listing of 1 000 autopsied cases collected and classified by Maude Abbott Because of its historic interest and value pathologically her classification and figures have been retained in this edition but the tabulated insert has been omitted

Mention need be made herewith only of two rare anomalies incompatible with life namely acardia (absence of heart) and hemicardia (absence of half the heart) these conditions were reported by Maude Abbott in 15 cases of an early series of hers of 850 autopsied cases (1928)

Incidence We still await adequate statistical information about the absolute and relative incidence of congenital cardiovascular disease in various parts of the world Our current impression is that it is found everywhere and in about the same total incidence but that it varies a good deal relatively depending on how much heart disease there is in general and so far as children are concerned on how much rheumatic heart disease there is in any district or community Statistics already available but as a rule still crude indicate a low total incidence averaging well under 1 per cent of all deaths An analysis of 34 023 unselected autopsies in Boston showed congenital cardiovascular disease in 1 33 per cent but this figure dropped to 0 5 per cent after the age of two (Gelfman and Levine 1942) An incidence of 0 9 per cent of con-

genital heart disease among 15 597 autopsies was reported by Clawson (1944) of this lot of 141 infants 18 were stillbirths and 83 died in the first five months of life only 30 cases (21 3 per cent) surviving after their first year A clinical series of 31 771 medical outpatients in Copenhagen contained 85 cases (0 27 per cent) diagnosed as congenital heart disease among 4 746 individuals with cardiovascular abnormalities (a relative incidence of 1 8 per cent) (Thordarson 1947) In a clinical series of cardiac patients under the age of twenty years in New England 6 per cent were found to be of congenital origin (White and Jones 1928) this figure would doubtless have been higher had more young infants been included since many of those severely involved die very young In California some years ago (1936) it was noted that the ratio of congenital to rheumatic heart disease was very different from that in New England being very much greater recent statistical information confirms the earlier figures among San Francisco school children there bein 0 19 per cent with congenital heart disease and 0 24 per cent with rheumatic heart disease a ratio of about four to five while the ratio in New England was once about one to ten until recent years when with the decrease of rheumatic heart disease and the increase of congenital cardiovascular cases seeking help the ratio has changed in New England to about two congenital to three rheumatic (actually 165 of the former and 257 of the latter under the age of twenty years among 2 000 cardiac patients—White 1951)

Etiology *Cause* One of the three great advances in our knowledge of this kind of heart disease during the past decade not known when the third edition of this book was being prepared has been the first clear evidence of a causative factor the other two advances being more accurate diagnosis and surgical treatment respectively In the last edition certain guesses were mentioned including alcoholism syphilis trauma fetal endocarditis and defects in the germ plasm but there was no clear knowledge It is still quite possible that some of these factors and others not mentioned or even thought of may prove eventually to play a role but the one substantiated factor discovered in Australia a few years ago (Gregg 1941 Swan 1943) was not mentioned earlier This is German measles (rubella) a virus disease, which appears to result in a combination of congenital defects (cataracts cardiovascular anomalies and at times deaf mutism and mental maldevelopment) in a considerable percentage of instances in which the mother is affected during the first two to three months of pregnancy The exact percentage is not yet known but has been to date estimated to be from one quarter to one half of the cases or even more One of the most recent reports (Wesselhoeft 1949) cites 67 infants with congenital heart lesions born of 132 mothers who had had rubella during the first trimester of pregnancy More recently other viruses have been suspected of causing congenital defects of heart and aorta in the fetus during early pregnancy but accurate information about this is still lacking

Our newly acquired knowledge about rubella and congenital heart disease gives us our first real hope about preventative measures At present the first crude steps have been taken in the way of advice to terminate pregnancy if rubella occurs during the first trimester or to attempt to infect girls and

young women before marriage but of course the vital need is early cure and prevention of the viruses themselves Gamma globulin has been suggested but its value has not been substantiated as yet in the case of rubella

Not rarely the apparent scarring with fibrosis and contraction of the endocardium of the right ventricle involving especially the infundibular area and the pulmonary valve itself strongly suggests the possibility of fetal endocarditis If this should be proved to be true we may again have weapons against such involvement in the form of modern chemotherapy and penicillin and its like in fact it will be of interest to determine whether in the future there may be a decrease in the incidence of infundibular and pulmonary stenosis associated with the current extensive use of these new therapeutic agents during pregnancy On the other hand the white fibrotic thickening of the endocardium per se as in the case of congenital anomalies of the coronary arterial circulation (in particular when the left coronary artery arises from the pulmonary artery) is ascribed best to the effect of prolonged anoxia

Sex There is a curious relationship of sex in certain congenital cardiovascular defects In the largest series of cases on record (1 000 cases with the sex stated in 859 Abbott 1931) the ratio of males to females was 58 to 42 it happened that in some of the individual lesions of this series the sexes were about evenly divided but pericardial defects (21 males to 9 females) cor biloculare i e two chambered heart and triloculare i e three-chambered heart (17 to 10) defects of aortic septum (28 to 11) transposition of arterial trunks (42 to 18) anomalies of the semilunar valve cusps (32 to 5) and coarctation of the aorta (60 to 19) were much commoner in the male while simple patency of the ductus arteriosus was more common in the female (55 to 29) and in the 53 cases of true atrial septal defect studied by Bedford Papp and Parkinson (1941) there was a female preponderance of 4 to 1 More cases however are needed to allow one to be at all certain of these proportions Recently the large series of cases of ductus patency operated upon by Gross (personal communication January 1950) gives a ratio of 276 females to 120 males and of coarctation of the aorta by Reifenstein et al (1947) gives one of five males to one female

Age Congenital heart disease may be found at any age but it is commonest of course in the infant and young child because many of the victims survive but a few years at the most and often only a few days or months The diagnosis is much more difficult however in very young children than at an older age because of the absence or paucity of symptoms and signs this explains why the percentage of accurate clinical diagnoses can be and often is higher in general hospitals than in children s or infants hospitals The age to which the patient lives depends largely on the degree of cyanosis and on the size of the heart markedly cyanosed children and those with very large hearts rarely survive to adolescence or to full adult age or at most beyond 30 years Delay in closure of a ductus arteriosus or of a foramen ovale during the first few months of life should not be interpreted as abnormal

Race Congenital cardiac defects have been reported in every civilized race

Social status Favorable social status and financial resources have not yet been shown to prevent congenital heart disease but they do favor longevity

Pathology The individual defects found in congenital heart disease will be discussed later in this chapter The most common defects in Abbott s post mortem series of 1 000 cases are interatrial septal defects (373 cases) interventricular septal defects (274 cases) simple patency of the ductus arteriosus (242 cases) pulmonary stenosis (151 cases), anomalies of the cusps of the semilunar valves (146 cases) coarctation of the aorta (adult type) (105 cases) anomalies of the great veins (94 cases), and complete transposition of the arterial trunks (74 cases)

Cases with combined cardiovascular defects are more common than those with the individual defects alone This is particularly true of interatrial septal defects pulmonary stenosis interventricular septal defects and patency of the ductus arteriosus In Abbott s series of 1 000 cases mentioned above an atrial septal defect was noted as the primary lesion in but 73 cases while it complicated other lesions in 300 cases, interventricular septal defects were classified as the primary lesion in 55 cases and as a complication of other lesions in 219 cases simple patency of the ductus arteriosus occurred primarily in 92 patients and as a complication in 150 others, and pulmonary stenosis occurred alone in but 9 cases while it was combined with other defects in 142 cases As a matter of fact it is to be expected that the defects should be complicated either through the simultaneous involvement of several areas of the heart in the embryonic maldevelopment or through the pressure effects secondarily resulting from a single lesion like pulmonary stenosis aortic stenosis or tricuspid atresia (complete closure) to keep patent the ductus arteriosus and defects in the septa between atria and between ventricles Only in certain instances as in the case of pericardial defects of primary congenital hypertrophy and of coarctation of the aorta do the defects tend to be isolated rather than in combination

The stage in the development of the embryo at which retardation or abnormality of growth occurs determines largely the type of congenital heart disease found later If the abnormality comes relatively early before the septa have appeared or have grown appreciably, the heart may remain as in the case of the primitive vertebrate heart (that of the fish) with but one atrium and one ventricle (cor biloculare) if the defect in growth begins later the heart may be three chambered as in the case of the reptile with two atria and one ventricle (cor triloculare biatriatum) Much less commonly the three-chambered heart has two ventricles and one atrium (cor triloculare biventriculare) [1] Later in the stage of embryonic growth after the septa have almost completely formed a defect may cause a permanent opening in the interatrial septum (which may be either a patent foramen ovale or a persistent ostium) or an aperture at the base of the interventricular septum just anterior to the unde-

[1] A unique freak of nature has been reported by Sinclair (1944) of a five-chambered heart with two atria a right ventri le and two left ventri les in a two-headed human monster with two aortas and two pulmonary arteries

fended space Also at this stage or earlier the common truncus arteriosus may not be completely divided into aorta and pulmonary artery leaving so called partial or complete defects of the aortic septum If in the course of growth of the embryo there is either (1) reversed torsion of the ventricular bend of the embryonic heart (2) malposition of the aortic septum in relation to the interventricular septum or (3) incomplete involution of the aortic part of the conus a transposition of the great vessels may result the aorta arising from the right ventricle and the pulmonary artery from the left

In the explanation of transposition of the great vessels in particular Spitzer s important phylogenetic theory deserves a leading position (1923) Harris and Farber (1939) have written about it as follows

Spitzer s main contribution is a theory of normal cardiac development The fundamental postulate of that theory is the orderly development of the organ as a unit in response to the varying conditions forces and demands in a series rising from fishes to birds and mammals It admits of no fortuitous variations which disregard the phylogenetic interrelations of these groups

With the advent of pulmonary respiration in phylogeny a very much greater volume of blood must pass through the heart Bending alone becomes inadequate to compensate for the lengthening tendency and torsion must take place The original right bend initiates the torsion to the right and the bulbar elements are thrown into a clockwise spiral Since the heart is fixed at both ends detorsion must take place and a counter clockwise spiral must be present at the opposite or venous end

"According to Spitzer this is the most important stage in cardiac development *Without it no advance could take place with faulty degrees of torsion the most bizarre anomalies result* The concept of torsion recur repeatedly through Spitzer s hypothesis and its importance cannot be underestimated The septum formation must not only separate the pulmonary and systemic circuits but also cross the circuits so that systemic venous blood enters the pulmonary artery and oxygenated blood passes out through the aorta A straight septum could only cause the circuits to exist side by side as in cases of complete transposition Torsion conditions the necessary spiral at the arterial end and thus permits the crossing over of the circuits In order that the countertorsion may not undo this effect the countertorsion must take place *peripheral* to the entrance of the pulmonary veins Furthermore it is through the torsion that the course of the longitudinal folds along which the blood flows easily is directed more or less into the current The forces residing in the blood stream may then work on the folds stimulate them to grow and cause them to develop into septums

A failure in development of the conus arteriosus or perhaps an infection involving it or its valve cusps after it has become differentiated into the infundibulum of the right ventricle results in pulmonary valve or oftener infundibular stenosis or atresia If this stenotic defect comes late it may occur as the only ventricular abnormality but this rarely happens generally it develops early along with failure of the interventricular septum to close completely with diversion of the blood into the aorta from the right ventricle in

a variable but usually considerable degree In most of such cases the aorta is dextroposed overriding in varying extent the ventricular septal defect and best explained by Spitzer s theory It is this combination of pulmonary stenosis interventricular septal defect dextroposition of the aorta and hypertrophy of the right ventricle that is more commonly found than any other cardiac condition in children (over a year old) and adults with cyanosis resulting from congenital heart disease This is the so called tetralogy of Fallot described by Stensen (Steno) in 1672 Sandifort in 1777 Hunter in 1784 Farre in 1814 Gintrac in 1824 and Peacock in 1858 but analyzed more completely as a clinical entity by Fallot in 1888

Fallot A Contribution a l anatomie pathologique de la maladie bleue (cyanose cardiaque) *Marseille med* 1888 XXV 77 138 207 270 341 and 403

Fallot s conclusions are as follows (translation by myself)

1 Clinicians have until now considered the precise diagnosis of the anatomic lesions of congenital heart disease with cyanosis (la maladie bleue) as almost impossible and to be expressed in the form of an entirely vague and uncertain hypothesis From observations that we have assembled it appears on the contrary that congenital heart disease with cyanosis above all in adults is the result of a small number of perfectly definite cardiac malformations

2 Of these malformations there is one which in frequency surpasses all others since we have met it in almost 74 per cent of our observations it is this malformation then that the clinician will be justified in diagnosing and in so doing the chances of error which he will run will be relatively few

3 This malformation constitutes a true pathologic anatomic type represented by the following tetralogy (1) stenosis of the pulmonary artery (2) interventricular septal defect (3) deviation of the origin of the aorta to the right and (4) hypertrophy of the right ventricle almost always concentric in type At times there is an additional entirely accessory defect namely patency of the foramen ovale

4 One cannot at the present time attribute the maladie bleue to the persistence of the foramen ovale without direct opposition to the great majority of observed facts when the communication between the two auricles exists alone without any other associated cardiac lesion cyanosis does not result

5 From the historical point of view one finds in the writings of the last century (the eighteenth) and of the beginning of the present frequent observations of congenital heart disease with cyanosis the majority present the interesting combination of the various cardiac lesions mentioned above

6 Finally from the pathogenic point of view the theory that considers the interventricular communication as a simple phenomenon belonging to the group of recessive anomalies rests only on a superficial and inexact interpretation of the facts the incompletely developed septum in the victim of the maladie bleue can be considered in no way as the analogue of the false septum of vertebrate animals with communicating ventricles it appears much more logical and more in keeping with physiological laws to regard the entire series of cardiac anomalies enumerated above as the consequence of the stenosis of the pulmonary artery As to the cause of this pulmonary stenosis we believe that we should attribute it not to a simple arrest in development but rather to a pathological process occurring in the region

of the pulmonary valve and of the infundibulum just below it during intrauterine life"

Much rarer than the tetralogy of Fallot is another somewhat similar combination of congenital defects consisting of dextroposition of the aorta (which is quite likely the primary condition as indeed it may be also in the tetralogy of Fallot) interventricular septal defect large right ventricle and normal or increased size rather than stenosis of the infundibulum and pulmonary valve and artery (Eisenmenger 1897 Rosedale 1935) A new entity associated with persistent cyanosis from birth with clinical fluoroscopic and electrocardiographic findings very similar to Eisenmenger s complex with which it is likely to be confused has been recently described by Taussig and Bing (1949) This new entity includes transposition of the aorta and a partial overriding of a ventricular septal defect by the large pulmonary artery arising primarily from the right ventricle

Finally of the commoner defects coarctation of the aorta and permanent patency of the ductus arteriosus appear latest of all at birth or shortly after when the heart and great vessels have otherwise attained normal growth and relations they may then occur alone probably because they are late defects Patency of the ductus arteriosus may really be designated as a postnatal defect since normally the ductus does not close until the first few days weeks or months after birth the ductus arteriosus was closed before the age of 8 weeks in 88 per cent of 558 normal infants hearts and the foramen ovale prior to 12 weeks after birth in 87 per cent of this same group (Christie 1930) Recently Everett (personal communication 1951) has found that the foramen ovale closes sooner after birth considerably before the ductus arteriosus

Clinical classification of congenital cardiovascular disease Various attempts have been made to group the different congenital cardiac defects and their combinations in order to produce a useful clinical classification not following necessarily any embryologic or pathologic plan A classical arrangement is that of the division of the cases into three groups (Abbott 1924 1928 1936) this arrangement is shown slightly modified in details in the following plan It may be said that the greater the degree of cyanosis the more serious is the case

Table 4

CLASSIFICATION OF CONGENITAL CARDIOVASCULAR DISEASE (ABBOTT)

(Order based on degrees of oxygen unsaturation and duration of life in 1 000 autopsied cases analyzed by Abbott)

I *Cases without Abnormal Communications or Shunts between the Right and Left Sides of the Heart Acyanotic Group* The lesions of these cases cause varying degrees of cardiac strain from little or none to a great deal Here belong the following relatively unimportant defects as well as more important anomalies

A Less important group

1 Simple dextrocardia usually with the situs inversus No limitation of life unless there are other congenital cardiovascular defects

2 Anomalies of the pericardium Defects and diverticula Maximum age = 75 years mean age at death in 36 cases = 45 years

3 Anomalous chordae Maximum age = 84 years mean age in 23 cases = 43 years

4 Uncomplicated quadricuspid and bicuspid semilunar valves more often aortic than pulmonary bicuspid aortic valves are a frequent site for bacterial endocarditis and so cannot be considered to be wholly unimportant Maximum age = 80 years mean age in 44 cases = 34 years

5 Double atrioventricular orifices Maximum age = 71 years mean age in 9 cases = 37 years

6 Pure coarctation of the aorta of adult type Maximum age = 92 years mean age in 70 cases = 33 years

7 Anomalies of aorta (such as right aortic arch) of the aortic branches of the coronary arteries of the pulmonary arteries and of the great veins unless these are extreme Very variable duration of life but as high as 87 years with double aortic arch (and as low as 3 months with left coronary artery arising from the pulmonary artery)

B More serious group

1 Ectopia cordis (extrathoracic heart in the abdomen) extra abdominal ectopia cordis does not allow survival for more than a few days Maximum age = 15 months mean age in 7 cases = 1 month

2 Primary congenital hypertrophy of the heart Maximum age = 4 years mean age in 15 cases = 10 months

3 Pure subaortic or aortic stenosis which exerts a considerable strain on the left ventricle Maximum age = 58 years mean age in 23 cases = 13 years

4 Pure mitral stenosis very rare Maximum age = 27 years mean age in 6 cases = 5½ years

5 Pure coarctation of the aorta of infantile type maximum age = 9 months mean age in 9 cases = 1¾ months

II *Cases of Arteriovenous Shunt with Possible Terminal or Transient Reversal of Flow (Cyanose Tardive)* In these cases arterial blood ordinarily enters the pulmonary circulation while venous blood rarely enters the systemic circulation Potentially cyanotic group

1 Patent ductus arteriosus Maximum age = 66 years mean age in 92 cases = 24 years

2 Localized defects of aortic septum (communication between base of aorta and pulmonary artery or base of right ventricle) Maximum age = 48 years mean age in 10 cases = 14 years

3 Localized defects of the interatrial septum including widely patent foramen ovale persistent ostium primum and persistent ostium secundum Maximum age = 70 years mean age in 68 cases = 27 years

4 Localized defects of the interventricular septum Maladie de Roger (Roger 1879) Maximum age = 49 years mean age in 50 cases = 14½ years

III *Cases of Venoarterial Shunt (Morbus caeruleus) (Maladie bleue)* Here venous blood in considerable quantity enters the systemic circulation Cyanotic group

A. Slight to moderate cyanosis

1 Defect of interventricular septum with dextroposition of the aorta Maximum age = 48 years mean age in 7 cases = 25 years

2. Cor triloculare biatriatum. Maximum age = 35 years mean age in 13 cases = $7\frac{3}{4}$ years

3 Pulmonary stenosis with patent foramen ovale Maximum age = 57 years mean age in 16 cases = 18 years

4 Tricuspid stenosis Maximum age = 28 years mean age in 3 cases = 15 years

5 Tricuspid atresia (imperforation from α privative not and τρῆσις perforation) with septal defects Maximum age = 56 years mean age in 16 cases = $5\frac{1}{2}$ years

B Moderate to marked cyanosis

1 Pulmonary stenosis with defect of ventricular septum and dextroposition of aorta (tetralogy of Fallot 1888 the fourth element of the tetralogy being right ventricular hypertrophy) Maximum age = 59 years 8 months mean age in 85 cases = 12 years

2 Pulmonary atresia with defect of ventricular septum and dextroposition of the aorta Maximum age = 30 years mean age in 30 cases = 5 years

3 Transposition of arterial trunks with defect of ventricular septum Maximum age = 16 years mean age in 17 cases = $2\frac{1}{4}$ years

C Extreme cyanosis

1 Cor biloculare with transposition of arterial trunks Maximum age = 16 years mean age in 2 cases = 9 years

2 Persistent truncus arteriosus (complete defect of aortic septum) with localized defect of interventricular septum Maximum age = 25 years mean age in 21 cases = 4 years

3 Cor biloculare with persistent truncus arteriosus (complete defect of cardiac and arterial septa) Maximum age = 14 days mean age in 5 cases = $6\frac{1}{2}$ days

4 Complete transposition of arterial trunks without defect of ventricular septum but with interatrial septal defect or patency of the ductus arteriosus Maximum age = 11 years mean age in 32 cases = 6 months

5 Pulmonary atresia with closed ventricular septum defective atrial septum and patent ductus arteriosus Maximum age = 20 years mean age in 10 cases = $1\frac{3}{4}$ years

6 Mitral atresia with aortic aplasia (lack of development from α privative not and πλάσσειν to form) defect of atrial and ventricular septa and patent ductus arteriosus Maximum age = 37 years mean age in 5 cases = 10 months

7 Aortic atresia transposition of arterial trunks closed ventricular septum patent ductus arteriosus Maximum age = 15 weeks mean age in 12 cases = 2 months

A practical clinical classification which the author has recently found very helpful is presented in Table 5

Symptoms Congenital heart disease may be present without any symptoms whatsoever if there is no venoarterial shunt or especial strain on the heart such is commonly the case when there is but a slight to moderate degree of

Table 5

DIAGNOSABLE CONGENITAL DEFECTS OF HEART AND GREAT VESSELS—1960

			DEFECT	SYMPTOMS	SIGNS
I INTRACARDIAC	A NONCYANOTIC	a) WITHOUT A SHUNT	1 AORTIC OR SUBAORTIC STENOSIS	O	G d 5 rtl sub rtl y t lle murmur a d th ill
			2 PULMONARY STENOSIS	O	C de 5 p lm n y s t lle murm d thrill
		b) WITH A SHUNT	3 ATRIAL SEPTAL DEFECT	Slight t m der t h l dy p ea	Grad 2 t 3 p lm nary y t ll murm r P ++
			4 VENTRICULAR SEPTAL DEFECT	ith m ll defect. dysp a ith larg es	Grad 5 s st lle m mu d th ill l f ternal bo der 4th pace
	B CYANOTIC		5 TETRALOGY OF FALLOT	Ret d d g wth I asily e h ust d I p a Sy p l tenden y	Cy l d fl g l bbl Gr d t 4 p lm ry s t ll murm
			6 PULMONARY STENOSIS +ATRIAL SEPTAL DEFECT	Slight t moderat he ic dy p ea	Cy l d fl er cl bbi g d l pi g i l il ih od (d 4 t 5 p lm ry s t ll murmur d thrill
			7 EISENMENGER COMPLEX	S m as f 5 d hem pty is	Cy osl a d l bbi g M y b murm
			8 TRICUSPID ATRESIA	S m as f 5	S me as f
			9 TRANSPOSITION OF THE GREAT VESSELS	S me as f 5	Deep cy osis d l bbi g V y larg h rt Heart f il
			10 TAUSSIG BING SYNDROME	Same as f 5	S me as for 7
II EXTRACARDIAC (N ncya tic)			11 COARCTATION OF AORTA	O	Hypertensi in rm d hypot i l legs I creased i ter ost l p l A rtl ti us murm al g pi
			12 PATENT DUCTUS ARTERIOSUS	O	C ti u pulm ary m rm ften f ll p ls pressur
			13 VASCULAR RING	Dy ph gia F eq t p lm ry I fecti	O

C ngenital heart block and cor nary omalies (both ery ar) m y b diagnosabl by lectrocardiogr m
*Tr nspositio f rt a d p rtial erridi g f tricul r sept l d fect by th large pulmonary artery arisi g primarily from th right entri le.

Table 5—Continued

DIAGNOSABLE CONGENITAL DEFECTS OF HEART AND GREAT VESSELS—1950

X RAY	ECG	BLOOD	CARDIAC CATHETERIZATION	SURGICAL RELIEF
Normal	Normal or Left ventricular hypertrophy	Normal	Normal	O
Pulmonary artery bulge enlarged pulmonary vascular markings usually decreased	Right ventricular hypertrophy + +	Normal	Pulmonary artery pressure less than pressure in right ventricle	Valvulotomy
Very large pulmonary artery and lung hiluses. Heart slightly enlarged	R V H + +	Normal	Increased oxygen in right atrium Increased pulmonary artery pressure	Beginning
Normal as [illegible] defects [illegible] heart may be enlarged	Usually Normal	Normal	Increased oxygen in right [illegible]	Beginning
Coeur en sabot with pulmonary [illegible] fields as a rule decreased with [illegible] bronchial arteries rarely increased	R V H + +	Polycythemia and increased hemoglobin	Catheter obstructed in pulmonary [illegible] and easily enters aorta. Decreased pulmonary blood pressure	Partially correct (Blalock [illegible])
Much as in the case of the tetralogy of Fallot (see above)	R V H + +	Polycythemia and increased hemoglobin	The interatrial septal defect may be entered by catheter. No passage between right ventricle and aorta as in the Tetralogy of Fallot. Stenosed pulmonary ostium	Probably valvulotomy
Normal or prominent pulmonary arc and right ventricle	R V H +	Same as 5	Catheter enters either aorta or pulmonary artery. Increased pulmonary pressure	O
Small right ventricle and pulmonary artery	L V H	Same as 5 and 6	Catheter enters left atrium [illegible] ventricle	Partially correct (Blalock [illegible])
Both ventricles may be enlarged. Great vessel shadow narrow [illegible] and wide in left [illegible]	R V H Usually	Same as 5	Catheter enters aorta from right ventricle	Operation (Blalock + Interatrial septal-defect)
Large right ventricle. Normal pulsating pulmonary arteries	R V H +	Same as 5	Catheter enters aorta from right [illegible] Catheter enters pulmonary artery also	Operation (Blalock + Interatrial septal defect)
Small aortic knob. Ribs notched	Normal hypertensive pattern	Normal	Normal	+
Slight prominent pulmonary [illegible]	Normal	Normal	Increased [illegible] in pulmonary artery. Increased pulmonary pressure ±	+
Compression of esophagus and trachea. Wide right aortic arch	Normal	Normal	Normal	+

uncomplicated patency of the ductus arteriosus coarctation of the aorta, or pure interventricular or interatrial septal defect On the other hand there may be marked symptoms if serious congenital cardiovascular lesions are present especially those attended by marked or extreme cyanosis (Groups III B and III C of Abbott s classification) and those with primary congenital hyper trophy marked coarctation of the aorta or pure stenosis of any of the valves

The symptom most commonly found is dyspnea particularly on exertion This dyspnea is of all grades occurring in the case of atrial septal defects as the result of overloading the pulmonary circulation and thus leaving too little room in the lungs for air and in the morbus caeruleus in paroxysms due probably to temporary increase of the amount of venous blood shunted into the systemic circulation which leads in turn to the appearance or increase of cyanosis Often there is but little dyspnea hardly noticeable which may show itself simply as an increase in respiratory rate Dyspnea was noted in 320 of Abbott s series of 1 000 cases of congenital heart disease

An interesting symptom doubtless related to both dyspnea and weakness is the frequent squatting during short walks or other exercise characteristic of children with the morbus caeruleus commonly the tetralogy of Fallot

Along with the higher grades of dyspnea cough is common hemoptysis is rare but may occur if there is pulmonary vascular engorgement from obstruc tion polycythemic congestion or heart failure Polycythemia may also give rise on occasion to epistaxis

Next in frequency after the respiratory and pulmonary symptoms are those of cerebral nature due chiefly to anoxemia but in the case of considerable polycythemia they are also due to the sluggish circulation and to cerebral thrombosis Weakness faintness headache dizziness syncope convulsions and coma delirium mania and transient or persistent paralyses have all been noted particularly in the cyanotic group of cases with congenital heart disease The greater the degree of cyanosis the greater is the likelihood of such cerebral seizures The cerebral manifestations may last from a few seconds to days at a time they often mean that the patient has been overtaxing his reserve In some cases they recur at intervals of a few days weeks or months for many years Not rarely they are the cause of death in the cyanotic cases Paradoxical cerebral embolism in cases with septal defects is responsible on occasion for abscesses of the brain

Gastrointestinal symptoms in congenital heart disease are not important except for the dysphagia caused by some anomalies of the aorta and its branches especially a right aortic arch Faulty circulation to the abdominal viscera may occasion anorexia nausea vomiting hematemesis tympanites constipation and combinations labeled biliousness If congestive failure supervenes an increase of such symptoms is common due especially to en gorgement of the liver

Other symptoms are infrequent except for the complaint of coldness of hands and feet with cyanosis tingling in the extremities and abnormal sus ceptibility to infections especially of respiratory nature Palpitation is some

times complained of it is rarely severe Pain is very rare compared to dyspnea

Signs Often there are no signs of congenital heart defects outside of the heart and sometimes there are none even in the heart itself

Of all general signs only one is both common and important and that is cyanosis found in slight to marked degree in less than half of the cases of congenital heart disease (noted in 475 cases of Abbott s series of 1 000 doubtless an exaggerated proportion because cyanotic cases attract much more attention than noncyanotic) It may be terminal only due either to a reversal of flow between the sides of the heart through a shunt or to congestive failure or to both it was terminal in 124 of Abbott s series of 475 cyanotic cases It is particularly likely to be delayed in appearing after birth but it may become very intense in late childhood and in adult life giving rise to the terms morbus caeruleus and maladie bleue (blue disease) In Chapter 4 cyanosis has already been discussed here it need only be reiterated that it is dependent on three factors (1) the shunt of venous blood into the systemic circulation which shunt must be about 30 per cent of the total to pass the threshold for cyanosis (2) the dilatation of skin and mucous membrane capillaries with peripheral slowing of the blood stream and (3) insufficient oxygenation of the blood in the lungs The first two of these three factors are commonly present in the cyanotic group of cases of congenital heart disease and sometimes the third factor is also added if there is engorgement of pulmonary blood vessels such as occurs in cases of atrial septal defects with overloading of the lesser circulation or if there is pulmonary arterial and arteriolar sclerosis due to pulmonary hyperemia or hypertension or with increased viscosity of the blood in polycythemia, or in the rare cases of failure of the left ventricle and of congenital mitral stenosis A blueness of the eye grounds cyanosis retinae may be a relatively early sign of the morbus caeruleus

The next most characteristic and constant sign in the severe cases that is in those with well-marked and chronic cyanosis is clubbing of the fingers and toes (Figure 63) This was noted in 132 of Abbott s series of 1 000 cases It varies greatly in degree as does cyanosis and like cyanosis is not frequent in the youngest infants or children it develops later than cyanosis

Malnutrition and faulty development are not necessary accompaniments of congenital heart disease even of the severer types but they have frequently been found. In Abbott s series delayed development was noted 150 times Faulty cerebral growth mental retardation and Mongolian idiocy have been occasionally associated with congenital heart disease Arachnodactyly consisting of spider like fingers (and toes) and elongation of the entire body is seen in rare cases of congenital heart disease and hardly if ever occurs without cardiovascular defects mostly atrial septal and aortic wall defects

Edema of lungs and of legs ascites and congestion of the liver occur in congenital heart disease only if congestive failure supervenes

Cardiac examination Physical examination of the heart yields signs dependent on the type and degree of the congenital defects There may be little or no evidence of trouble in the heart even in some of the cases with such

serious lesions as the tetralogy of Fallot (pulmonary *stenosis* ventricular septal defect dextroposition of the aorta and big right ventricle) (*Figure 64*) There usually is but little enlargement in some cases however the apex im pulse and the left border of dullness are well beyond the *midclavicular line* more increased transversely in the fifth intercostal space than downward in the sixth or seventh spaces since the right ventricle is enlarged more often than the left in congenital heart disease (Figure 71 opposite page 318) There may be increase in dullness to the right of the sternum usually there is not unless the heart shows well marked general enlargement or an abnormal position (dextrocardia) The region of the great vessels shows no abnormal dullness except with a patent ductus arteriosus or an atrial septal defect when the pulmonary artery may show itself to be enlarged by percussion in the

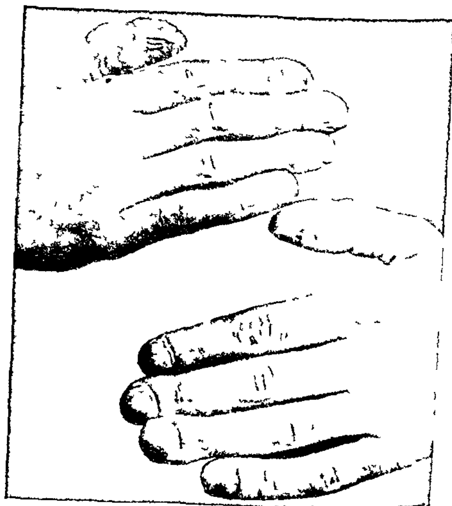


FIG 63 Photograph showing clubbing of the fingers in the morbus *caeruleus* (maladie bleue)

second and third intercostal spaces at the left of the sternum Palpation usually reveals a more or less normal apex impulse Occasionally there is felt a systolic thrill located at the left border of the sternum midway between upper and lower ends if there is a pure interventricular septal defect somewhat higher if there is pulmonary or infundibular stenosis and maximally in the second right intercostal space if there is congenital subaortic or aortic stenosis There often is a continuous thrill at the left border of the upper sternum in cases of patent ductus arteriosus

Auscultation may reveal no abnormalities even with serious congenital

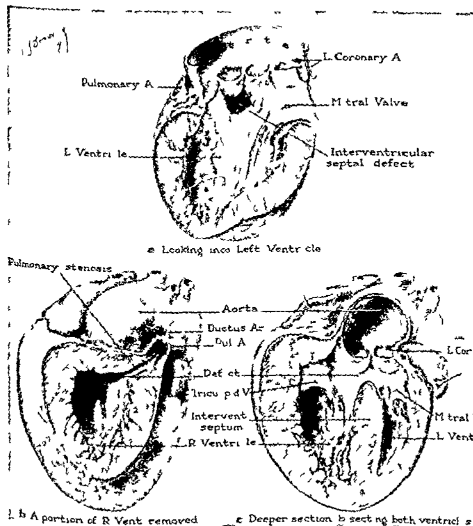


FIG 64 Photograph of congenital heart showing very large right ventricle in tetralogy of Fallot (Kindness of Dr Helen Taussig Johns Hopkins Hospital Baltimore and The Commonwealth Fund New York City)

defects There may or may not be murmurs When murmurs occur they are as a rule systolic in time and loudest just to the left of the sternum where they may be very limited in extent, located in the first intercostal space in some cases of patency of the ductus arteriosus, in the second space with pulmonary stenosis in the third space with infundibular stenosis and in the third and fourth interspaces in most cases of interventricular septal defect (Roger s murmur) Diastolic murmurs are uncommon as solitary findings they have been noted where the pulmonary or aortic valve has been defective and in rare cases of patency of the ductus arteriosus or larger interatrial septal defects They may also accompany the systolic murmurs of dilated pulmonary arteries in cases of large atrial septal defects when they are the result of a stretching of the pulmonary valve rings—such murmurs are likely to be transient like the Graham Steell murmur A continuous murmur roaring and machine like in character extending throughout systole and diastole with systolic accentuation is not infrequently found in the first three intercostal spaces just to the left of the sternum maximal in the first space When present it is usually pathognomonic of patency of the ductus arteriosus if venous hums transmitted from the neck and very rare and obvious arteriovenous aneurysms of the great vessels are excluded such exclusion is easily accomplished

It is important to remember that murmurs and thrills are very variable accompaniments of congenital heart defects the larger the defect the less likely are murmurs and thrills to be found A narrow caliber of patent ductus arteriosus or of interventricular septal defect is much more likely to give rise to murmur and thrill than is a large and much more serious patency which may show no murmur or thrill at all In the case of a stenotic lesion like pulmonary stenosis or coarctation of the aorta the greater the degree of stenosis the more frequently are murmur and thrill to be found but here too when the defect is extreme and there is complete atresia murmur and thrill will be absent One must use much judgment therefore in the analysis of the findings on physical examination of the heart in congenital cardiac disease it is necessary to depend more on other methods of examination

Heart sounds rate and rhythm are generally not abnormal in cases with congenital cardiovascular defects except in the case of pulmonary stenosis when the second sound in the second left interspace tends to be much diminished while with ductus patency or atrial septal defect it is usually accentuated With failure the sounds may decrease and the rate may increase but marked disturbances are rare and arrhythmia is very uncommon Premature beats and paroxysmal tachycardia are seen infrequently Atrial fibrillation is very unusual There is one disturbance of rhythm however which is an important though rare accompaniment of congenital heart disease this is *heart block* A few cases of unquestionable congenital heart block are on record The block may be either partial or complete It has been thought to be associated with interventricular septal defect and in three cases with postmortem study this defect was found to be extensive in degree (Wilson and Grant 1926 Yater 1928 and personal communication Abbott 1930)

Blood pressure The systolic blood pressure in congenital heart disease is not remarkable It tends to be low especially where there is an atrial septal defect or subaortic (or aortic) stenosis or much polycythemia and peripheral vasodilatation then the pulse pressure also is low An interesting finding of a fullness of pulse due to low diastolic pressure is to be noted in some cases of patency of the ductus arteriosus of extensive degree where a hydrodynamic situation exists somewhat comparable to that in the case of aortic regurgitation Also it is an important fact for diagnosis that with coarctation of the aorta the blood pressure (systolic and pulse pressure) in the upper extremities is higher than that in the lower extremities sometimes to a marked degree when the coarctation is extreme

Roentgenologic study Roentgen ray study of the heart and great vessels in congenital heart disease may be a great aid but it is sometimes of no help at all and serious cardiovascular defects may exist with no clear indication of their presence by roentgen ray Positive findings by this method of examination may be however the only clue to trouble either to its existence or to the particular lesion or lesions especially in differentiating left heart involvement from right and in revealing abnormalities of the great vessels Right ventricular enlargement may be revealed more by the so-called *coeur en sabot* or wooden shoe shape of heart shadow than by any increase in size of the cardiac silhouette (Figure 72 page 319) this is found especially when the pulmonary artery is hypoplastic (small) as in the tetralogy of Fallot but not when it is large even though the right ventricle is very big as with an atrial septal defect Marked enlargement of the whole heart shadow is characteristic of congenital idiopathic hypertrophy of coronary anomalies (the left arising from the pulmonary artery) and of von Gierke s glycogen storage disease (see page 323) Undue prominence of the shadow of the pulmonary artery may confirm the diagnosis of patent ductus arteriosus (see Figure 80 page 339) When there is no characteristic murmur of patency of the ductus arteriosus bulging of the pulmonary arc as seen by roentgen ray strongly favors the diagnosis of a defect in the septum between the atria and the larger the bulge the more likely is the latter defect Errors have frequently arisen in the past from relying on roentgenologic rather than on auscultatory evidence of ductus arteriosus patency Marked dilatation of the vessels in the lung hilus shadows helps to establish the diagnosis of an interatrial septal defect (see Figure 68 page 313)

Increase in the shadow of the ascending aorta is especially the rule in the tetralogy of Fallot where the aorta is both dextroposed and abnormally capacious it may also be found to a lesser degree with coarctation of the aorta Decrease in the ascending aortic shadow is common in the case of atrial septal defects and with aortic stenosis Absence of the aortic arch shadow may be found if there is considerable coarctation of the aorta or a right sided arch may be visible The esophagus and trachea may be displaced forward by a right sided aortic arch and compressed by a vascular ring And finally notching of the ribs may be evident due to dilated intercostal arteries in cases of coarctation of the aorta (see Figure 77 page 332)

Electrocardiographic examination In some cases of congenital heart disease the electrocardiogram is normal or so slightly divergent from the normal that it is in no way helpful Even negative findings are useful however since they tend to rule out right sided lesions when there is uncomplicated defect of the interventricular septum patency of the ductus arteriosus or coarctation of the aorta There are three conditions where the electrocardiogram is especially helpful and shows characteristic changes The more common of these three is right ventricular enlargement, usually associated either with pulmonary stenosis most commonly found in that combination of defects already described as the tetralogy of Fallot or with interatrial septal defect These conditions give rise to right ventricular preponderance often of marked degree In fact the greatest degree of right ventricular preponderance known is found in congenital heart disease With this abnormal right axis deviation there is found usually an abnormal increase of amplitude of the *P* (atrial) wave The second characteristic electrocardiographic pattern is that showing abnormal left axis deviation due to enlargement of the left ventricle in the rare cases of tricuspid atresia here the electrocardiogram may be the chief clue in the differentiation from the tetralogy of Fallot since both conditions cause considerable cyanosis and finger clubbing The third characteristic electrocardiographic finding is in the case of mirror picture dextrocardia the so-called heterotaxy (ἕτερος opposite and τάξις arrangement) whether complete or isolated (that is with or without abdominal visceral transposition also), here Lead 1 of the electrocardiogram is completely inverted and Leads 2 and 3 are reversed (Figure 65) Isolated congenital dextrocardia as a matter of fact has not been found to occur without other more important congenital cardiovascular defects (Roesler 1930) It is of great importance to be certain that this electrocardiogram is caused by the position of the heart and not by art fact due to crossing of the first two lead connections If as occurs in some cases dextrocardia is associated with some defect which results in right ventricular enlargement then the electrocardiogram will indicate a marked degree of abnormal left axis deviation but with inverted *P* waves in Lead 1 In cases of the two-chambered heart (cor biloculare) or of the three chambered heart with one ventricle (cor triloculare biatriatum) there tend to be biphasic *QRS* waves of wide amplitude in all three classical limb leads and in the precordial leads Finally as noted above there are rare cases of congenital heart block either complete or partial requiring electrocardiography for confirmation it is of interest that the ventricular rate in cases of congenital complete heart block tends to be rather high in the fifties or sixties as a rule and so may obscure the disorder of rhythm until an electrocardiogram is obtained

Other data Urine Albuminuria is common in the severer types of congenital heart disease partly because of engorgement due to polycythemia less often because of slight to moderate congestion from cardiac insufficiency

The blood Unless there is cyanosis or infection the blood cell counts and hemoglobin will be normal With a complicating infection polymorphonuclear leukocytosis is of course expected With cyanosis and a shunt of venous blood

into the systemic circulation a polycythemia is found increasing in degree as the shunt and cyanosis increase A red blood cell count of 6 or 7 millions is common in cases classed as the morbus caeruleus and in extreme cases even 10 11 and 12 million erythrocytes have been reported Along with this increase of red cells there is an increase of hemoglobin which usually runs

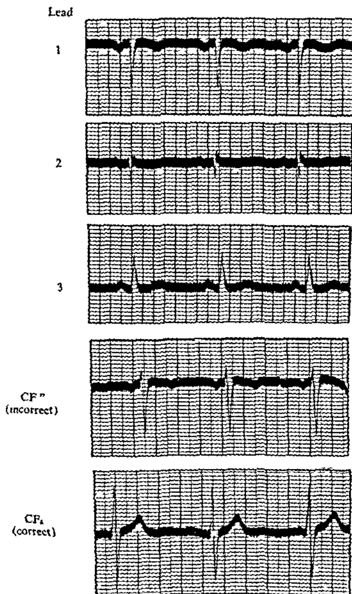


FIG. 65 Electrocardiogram (four leads) in a case of congenital dextrocardia with complete situs inversus and without other congenital defects The first Lead "CF" taken (labeled "incorrect" above) was erroneously obtained from the left side On discovery of the dextrocardia the correct Lead CF was taken as shown above J G male age 30

parallel, to 110 120 130, and in rare cases up to 180 or 200 per cent (25 gm) The reason for these increases is obvious Since the oxygen saturation of the hemoglobin is low because of lack of contact of a large percentage of the red cells with oxygen in the alveoli of the lungs an increase in the number of red cells occurs in order to transport sufficient oxygen to the tissues The oxygen capacity may almost double while the oxygen saturation of the blood is nearly halved the result is close to a normal amount of oxygen in the blood under favorable circumstances

The viscosity of the blood is much increased in polycythemia since viscosity is controlled chiefly by the number of cellular elements in the blood It may be increased several fold This means more work for the circulation and peripheral vasodilatation occurs in part to allow a more complete oxygen distribution to the tissues and in part to relieve the strain on the heart The actual blood volume is also increased in polycythemia the amount depending on the degree of cellular increase

The amount of oxygen and of carbon dioxide in the blood has already been referred to (Chapter 10) It is normal in cases of congenital defects without unusual communications but there are two abnormal situations dependent on the direction of the shunt venoarterial and arteriovenous

Venoarterial shunts An abnormally low oxygen saturation of the hemoglobin of the arterial blood is common in the case of the defects which result in venoarterial shunts it may reach even the low figure of 58 to 62 per cent (*Talbott et al 1941*) *If about one third of the venous blood entering* the right heart chambers is shunted directly into the systemic circulation the percentage of blue-colored reduced hemoglobin in the arterial blood may be increased to 20 per cent instead of the normal 1 to 5 per cent (or 4 volumes per cent instead of the normal ½ to 1 volume per cent) passing the threshold at which cyanosis appears A greater shunt than this yields still more reduced hemoglobin in the arterial blood and a greater degree of cyanosis in the case already referred to with very low oxygen saturation of the arterial blood it was estimated that 75 per cent of the blood in the heart chambers traversed the right to left shunt (Talbott et al 1941) However it is possible for a smaller shunt than that of one third to produce cyanosis provided there is an abnormally high red cell and hemoglobin content It is not the percentage but the total amount of reduced hemoglobin whether originating by shunt in heart or lungs or by peripheral stasis that is primarily responsible for the abnorm l color of the blood made obvious by dilated capillary vessels If in the capillaries there are 5 gm or more of reduced hemoglobin per 100 cc of blood cyanosis will result With normal red cell and hemoglobin content 3 5 to 4 volumes of reduced hemoglobin in the arterial blood will yield 6 5 or more volumes per cent in the capillary blood (or 5 gm per 100 cc) With polycythemia and an *increased oxygen content capacity of the blood due to increased* hemoglobin the same amount of reduced hemoglobin may be present in the capillary blood to cause cyanosis even though the actual percentage of oxygen unsaturation of the arterial blood due to a smaller shunt may be only 10 or

15 per cent If it were possible for severe anemia and a very low hemoglobin content (and therefore a low oxygen capacity of the blood) to develop in cases of venoarterial heart shunts it might be impossible to reach the stage of cyanosis no matter how little the oxygen saturation of the arterial blood might be because as much as 5 gm of reduced hemoglobin could not be produced in 100 cc of capillary blood The occurrence of severe anemia in the morbus caeruleus is however not likely since it would seem to be incompatible with life

Two other factors often enter into congenital heart disease with a venoarterial shunt to decrease the oxygen content of the capillary blood One of these is the structural and functional state of the lungs a factor which even with cardiac catheterization makes difficult any accurate estimation of the amount of the shunt Polycythemia and thickening of the alveolar capillaries are inevitable accompaniments of advanced morbus caeruleus Failure of proper oxygenation of the blood in the lungs may add its effect to that of a venoarterial shunt in reducing the oxygen content of arterial and capillary blood and in causing cyanosis The second additional factor consists of the slowing of the peripheral circulation which decreases still further the oxygen content of capillary blood in the morbus caeruleus The content of oxygen in the venous blood follows that of the arterial blood in such cases but is several volumes per cent lower An interesting and important factor that helps to decrease the oxygen unsaturation of the blood in cases of right to left shunt is the development of a somewhat compensatory collateral bronchial circulation The bronchial arteries and their branches course along the bronchi and bronchioles parallel to the pulmonary arteries but with a much more tortuous course They may become considerably enlarged in cases of the morbus caeruleus particularly the tetralogy of Fallot and thus may bring a good deal of blood to the lungs for oxygenation This bronchial circulation may appear quite clearly in the x ray pictures of the chest even though the pulmonary artery and its branches are much diminished in such shadows

The carbon dioxide content of the arterial and venous blood in the morbus caeruleus tends to be low rather than high (as one might at first have expected it to be) This is probably due to increased ventilation whereby the carbon dioxide which is thirty times more diffusible than oxygen is pumped out of the blood in the lungs and also to a tissue acidosis from faulty metabolism (due to the poor circulatory state) with retention of bicarbonate in the tissues

An interesting effect of venoarterial shunts on tests of the rate of the circulation (see Chapter 10) is worthy of note In cases with such shunts in the absence of heart failure not only is arm vein to tongue arterioles time much reduced below the usual normal because of cutting out the lesser circulation from a good deal of the blood flow but the total round trip (arm to tongue or arm vein to leg artery) time may actually be or seem to be slightly faster than the arm to lung time as in tests with ether

Arteriovenous shunts The other particular influence of congenital cardiac defects on the blood gases is in the case of arteriovenous shunts particularly

atrial septal defects patency of the ductus arteriosus and interventricular septal defects If large enough these defects cause by their admixture of arterial with venous blood abnormally high oxygen and abnormally low carbon dioxide content of the venous blood entering the pulmonary circulation (Burwell Eppinger and Gross 1940 and 1941)

Cardiac catheterization Catheterization of the heart chambers and pulmonary artery has been discussed in Chapter 10 but one should add here that perhaps its most useful application is in the diagnosis of congenital defects a higher blood content of oxygen than normal is found in the right atrium in the case of an atrial septal defect in the right ventricle in the case of a ventricular septal defect and in the pulmonary artery in the presence of a patent ductus arteriosus Moreover, the catheter can be passed under fluoroscopy through an atrial septal opening into the left atrium or into the aorta in the tetralogy of Fallot (see Figure 56 pages 228 and 229)

Course and prognosis The course and prognosis of congenital heart disease vary with the type In cases with relatively unimportant lesions where there are no shunts for example abnormal chordae tendineae and valve cusps simple dextrocardia pericardial anomalies slight to moderate coarctation of the aorta and in cases with lesser degrees of arteriovenous shunt through uncomplicated patent ductus arteriosus or interventricular septal defect life may not be handicapped or shortened and with all these conditions old age has been comfortably reached with no cardiac disability due to these defects Even these lesions are however somewhat perilous because of the possibility of their being the site of bacterial infection especially of streptococcal nature This infectious invasion serious and in former days so often fatal is not rare particularly in the case of bicuspid aortic valves of ventricular septal defects and of patent ductus arteriosus in Maude Abbott s series 9 of 32 cases (28 per cent) of the first named 13 of 50 cases (26 per cent) of the second and 21 of 92 cases (23 per cent) of the last named developed subacute bacterial endocarditis or endarteritis Gelfman and Levine (1942) found the incidence of acute and subacute bacterial invasion in patients over the age of two years with the more common congenital cardiovascular defects as follows ventricular septal defects (Roger s disease) 57 1 per cent of 14 cases patent ductus arteriosus 28 6 per cent of 14 cases pulmonic stenosis 29 4 per cent of 17 cases bicuspid aortic valves 21 2 per cent of 52 cases tetralogy of Fallot 28 6 per cent of 7 cases coarctation of the aorta 10 per cent of 10 cases and *atrial septal defects none among 45 cases*

In the case of the more serious defects the course is difficult and the prognosis grave Both the difficulty of the course and the seriousness of the prognosis depend on two factors The first of these factors is the degree of anoxemia which is indicated to a certain extent by the degree of cyanosis This anoxemia affects all organs of the body especially the brain and the heart The second factor is the amount of direct strain on the heart Two other points are to be remembered Cyanosis does not usually appear early in infancy and yet the prognosis at this early age may be bad Moreover, anoxemia

and cyanosis are not strictly comparable since there may be a sufficient quantity of oxygen in the blood for the tissues if there is a polycythemia and yet there may be also enough reduced hemoglobin to cause cyanosis This explains why many cyanotic individuals are not dyspneic

The most serious lesions like ectopia cordis abdominalis uncomplicated transposition of the great vessels the two chambered heart and pulmonary or aortic atresia with closed ventricular septum may be so crippling that a miserable existence is possible for but a few days weeks or months at best

Sudden unexpected death is not a rare termination in the case of infants and children with congenital heart disease even in those who show little or no evidence of the condition during life (Levinson 1941)

The less grave cases of the morbus caeruleus may occasionally survive to adult life or even into middle age if they live carefully and are fortunate enough to escape serious complications Some striking cases are on record of long survival especially one of a noted musician who lived a useful life to the age of 59 years and 8 months in spite of the tetralogy of Fallot and another of a woman with marked pulmonary valve stenosis and atrial septal defect who lived actively until she died of right heart failure at the age of 74 years and 11 months Both diagnoses were confirmed by postmortem examination and both patients showed cyanosis and clubbing of the fingers from early child hood (White and Sprague 1929 White Hurst and Fennel 1950) Limitation of activity is almost always enforced by the morbus caeruleus because of dyspnea weakness and cerebral symptoms

Complications The chief complications of congenital heart disease are in fections especially pneumonia cerebral attacks—syncope coma convulsions and hemiplegia due to thrombosis or hemorrhage—bacterial endocarditis or endarteritis and congestive heart failure These complications are often fatal An analysis of 453 autopsied cases of all ages of congenital heart disease in Boston hospitals gave a total incidence of 6 6 per cent affected by subacute bacterial endocarditis or endarteritis as compared with 16 6 per cent among those over the age of 2 years (Gelfman and Levine 1942) This dread disease is now fortunately in major part preventable or curable because of the advance in surgical therapy and of the introduction of penicillin An uncommon com plication in cases with septal defects is cerebral infarction or abscess from paradoxical embolism

Treatment In the first two editions of this book (1931 and 1937) it was stated that there is no curative treatment surgical or medical for congenital cardiac defects but notable advances have been made in the last twelve years in several particulars (1) patency of the ductus arteriosus is now curable by surgery (2) coarctation of the aorta can also be corrected surgically in nearly all young cases (3) a vascular ring constricting trachea and esophagus can be broken (4) certain instances of the morbus caeruleus in particular the tetralogy of Fallot can be greatly helped by surgery and (5) penicillin can cure many of the cases infected by the alpha hemolytic streptococcus And other advances are in the offing

In some cases of congenital heart disease no special care is needed though even the least serious case should be protected against infection to avoid complicating bacterial invasion and pneumonia. Since the teeth and gums harbor in particular the alpha hemolytic streptococcus, the cause of subacute bacterial endocarditis and endarteritis in the vast majority of cases, it is wise to protect by penicillin the patients with congenital cardiovascular defects who are to be subjected to dental extractions or other extensive treatment. 300,000 units should be given intramuscularly 1 hour before the dental treatment and again 3 hours after.

Tonsillectomy is probably advisable in childhood, though not in infancy, provided the tonsils are diseased and provided there is not too great a risk for operation. Protection from fatigue and care to provide suitable diet are to be urged for the cyanotic cases and for those with much heart strain. *Finally*, complications of congestive failure, cerebral lesions and *infections* are to be treated as such, by rest in bed, digitalis as required, penicillin and other measures. If the victim of congenital heart disease is well protected his life may sometimes be prolonged for many years.

Differential diagnosis. Congenital heart disease may resemble two other conditions, acquired heart disease and pulmonary disease. It is to be differentiated from the former by the history of involvement of the heart from birth if that is reliably obtained, and by the characteristic signs—certain murmurs, heart shape, cyanosis, clubbing of the fingers, and typical electrocardiograms when such exist (as described above), in a few instances the differentiation is very difficult. Acquired heart disease, especially rheumatic, subacute bacterial and coronary, may be superimposed on congenital cardiovascular defects.

It is more difficult to differentiate pulmonary disease, such as pulmonary fibrosis with emphysema or pulmonary endarteritis, when it is attended by cyanosis, polycythemia and clubbing of the fingers, from the morbus caeruleus of congenital heart disease, especially if the latter happens not to show characteristic murmurs, electrocardiograms or orthodiagrams. Great care must be taken in analyzing such cases.

The discovery of congenital anomalies elsewhere in the body favors somewhat the diagnosis of congenital cardiovascular defects when the differentiation of the type of heart disease is difficult or obscure.

The more common individual congenital cardiovascular defects should in the present day and age (in striking contrast to a generation ago) usually be differentiated with ease except in infancy. It seems likely that the ratio of diagnosability of individual defects during infancy to that after infancy is about 30 per cent as compared to 90 per cent. Rare defects are, however, as a rule undiagnosable.

INDIVIDUAL CONGENITAL CARDIOVASCULAR DEFECTS

It has become possible during the present generation clinically to recognize the majority of congenital cardiovascular defects and therefore they have

assumed an increasing importance in the practice of medicine They will be presented in the following order congenital malposition of the heart congenital abnormalities of the cardiac chambers and septal defects congenital myocardial disease congenital endocarditis and valvular defects congenital pericardial defects congenital anomalies of the great arteries and veins and congenital anomalies of the coronary arteries

CONGENITAL MALPOSITION

Congenital malposition of the heart includes dextrocardia and ectopia cordis

Congenital dextrocardia is of two main types occurring with about equal frequency (1) In the first type without transposition the heart is slightly rotated and rests in the right side of the chest The left chambers lie to the left and anteriorly the right chambers lie to the right and posteriorly and the apex is made up either of the right ventricle or of the right side of the common ventricle Almost invariably in this type there is some serious associated congenital anomaly like a single ventricle The prognosis and course of the congenital heart disease depend on these associated anomalies and not on the dextrocardia (2) The other variety of congenital dextrocardia is that attended by transposition of the chambers whereby the left chambers lie on the right side and form the right border and apex and the right chambers lie on the left side Almost invariably the abdominal viscera are also transposed (complete heterotaxy or situs inversus) With this type of congenital dextrocardia that is the mirror type there are usually no other congenital cardiac defects at least of serious nature unless the dextrocardia is isolated that is occurring without associated general transposition of other organs (Roesler 1930) Dextrocardia uncomplicated by other cardiovascular defects is unimportant clinically It is discovered accidentally on routine physical or roentgen ray examination or even by electrocardiography and in no way affects activity or duration of life A pathognomonic sign of this mirror type of congenital dextrocardia is electrocardiographic complete inversion of Leads 1 and aVR and transposition of Leads 2 and 3 aVL and aVF and of the precordial leads (Figure 65) An interesting complication of the situs inversus which may in some cases be regarded as a stigma of an associated congenital maldevelopment is bronchiectasis which was found in 5 of the 23 cases of the situs inversus (21 7 per cent) recorded at the Massachusetts General Hospital in the fifty years from 1886 to 1936 while of the general hospital population over that period of time bronchiectasis was diagnosed in but 0 3 per cent (Churchill and Adams 1937)

Ectopia cordis a very rare defect consists of the malposition of the heart outside of the thoracic cage either in the abdomen or actually projecting outside the body wall It is of academic interest only since attempts at surgical correction have as yet been unsuccessful and life is almost invariably very brief a matter of a few days or at best a few weeks

CONGENITAL ABNORMALITIES OF CARDIAC CHAMBERS SEPTAL DEFECTS

Congenital abnormalities of the cardiac chambers include complete and partial absence of atrial and ventricular septa These defects may be unimportant discovered only at postmortem examination after a long and active life and unsuspected before death or they may be of great importance permitting only a few hours or days of existence after birth The degree of the defect and complicating abnormalities determine the importance of each lesion

Atrial Septal Defects

Atrial septal defects are much more numerous than any other anomaly in congenital cardiovascular disease In Abbott s series of 1 000 cases there were 402 individuals with openings between the atria which included true (not slit like) patency of the foramen ovale (290 cases) persistent ostium primum in the lower part of the septum (36 cases) persistent ostium secundum in the upper part (19 cases) multiple defects (28 cases) and complete *absence of the septum in the biloculate heart (14 cases) or in the triloculate* heart with one atrium and two ventricles (15 cases)

Patency of the foramen ovale is of the least importance and greatest frequency of all congenital cardiac abnormalities The foramen ovale is a valve like opening between the atria developing from the ostium secundum of the embryo and functioning in fetal life to allow the passage of considerable blood directly from venous to arterial circulation without going through the lungs It closes soon after birth and usually becomes sealed within the first three months of life In many cases it remains anatomically slightly patent as a valve slit but as such it is functionally inactive When the slit opening is small the patent foramen ovale is of absolutely no importance but if it is moderately large and the right atrial pressure is much raised venous blood may pass into the left atrium and even occasion slight cyanosis Clinically unimportant patency of the foramen ovale has been reported in nearly one quarter of all autopsied cases (with a range from about one eighth to one third)

In a few cases the foramen ovale remains really patent and in such cases it may prove to be of some importance In one series of 500 hearts (250 from white and 250 from Negro subjects) probe patency of the foramen ovale was found in 85 cases (17 per cent) while in only 2 cases (0 4 per cent) did the valvula foraminis ovalis actually fail completely to cover over the foramen ovale (Seib 1934) Wide patency is usually associated with and probably caused by other more important congenital abnormalities such as pulmonary stenosis or transposition of the great arterial trunks or with acquired mitral stenosis and these other defects determine the course and prognosis Of a

The terms "atrial septum" and "ventricular septum are used interchangeably with inter atrial septum" and "interventricular septum" respectively

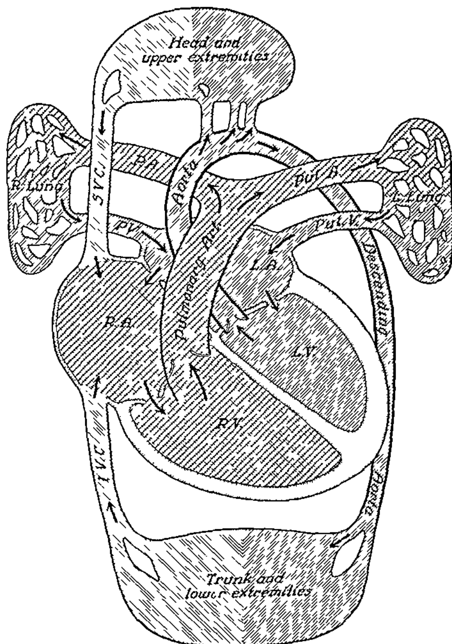


FIG 66 Diagram of atrial septal defect (Kindness of Dr Helen Taussig Johns Hopkins Hospital Baltimore and The Commonwealth Fund New York City)

series of 290 cases of patent foramen ovale (Abbott 1931) only 40 were instances of pure or primary patency

Atrial septal defects of importance are those that involve relatively large areas of the septum (1) The *primitive ostium primum* in the lower part of the septum (36 cases in Abbott s series of 1 000 individuals with congenital cardiovascular defects 18 of the 36 complicating other defects) or (2) the *primitive ostium secundum* (from which the foramen ovale develops) in the upper part of the septum (19 cases of Abbott s series 9 of which complicated other defects) or (3) *absence of the entire atrial septum* giving a three chambered or *triloculate heart* (*cor triloculare biventriculare*) if there are two ventricles or a two-chambered or *biloculate heart* (*cor biloculare*) if there is but one ventricle (15 cases of the former and 14 of the latter in Abbott s series) Females showed a slight preponderance (44 to 35) in these three categories of atrial septal defect in Abbott s series All these lesions are more serious than patency of the foramen ovale persist from an earlier stage of fetal life and are often complicated bv other anomalies Persistence of the ostium primum is not only more common than that of the ostium secundum but it is also much more serious (Figure 66 opposite page 310)

The explanation of the increase in size and work of the right heart chambers in these cases is that extra blood often in large amount enters the right atrium from the left atrium through the septal defect this direction of flow has been assumed to be due to a slightly higher pressure in the left atrium but Uhley (1942) has shown that an important perhaps the most important cause of this direction of flow is the effect of gravity the right atrium being anatomically situated below the left, the septum lying more or less horizontally

In the cases of persistence of the primary and secondary ostia there may be no symptoms or signs and the subjects may live fairly long lives though not so long as those with foramen ovale patency Enlargement and failure of the right ventricle are however common Loud systolic murmurs rarely accompanied by thrills are found in most of the cases chiefly in the pulmonary valve area Years ago they were ascribed to the septal defect itself but it has become evident that they are due to the dilatation of the pulmonary artery which is secondary to the increased pulmonary circulation or to a complicating mitral valve defect With large atrial defects the electrocardiogram shows marked right axis deviation (Figure 67) and the roentgen ray shows enlargement of the right atrium right ventricle and pulmonary artery and its branches large and small and also hypoplastic aorta (Figure 68) it is probable that in some cases at least twice as much blood passes through the pulmonary circulation as through the systemic Paradoxical embolism may occur Cyanosis is infrequent but may appear as an occasional or terminal event when the right atrial pressure becomes greater than that in the left atrium or constantly if there is a complicating pulmonary stenosis

An analysis of 53 cases of atrial septal defects 10 with necropsy control (Bedford Papp and Parkinson 1941) showed a preponderance of females in the ratio of 4 to 1 the age of death mostly from 30 to 50 years and the

cause of death in the autopsied cases congestive heart failure in 3 pulmonary infarction in 2 embolism (one paradoxical) in 2 subacute bacterial endocarditis (a very rare complication) in only 1, bronchopneumonia in 1 and surgical operation in 1 the upper part of the septum was involved in 8 of these 10 cases A pulmonary systolic murmur was found in 32 of the entire series and an accentuated pulmonary second sound in 31, followed by a diastolic murmur (probably due to a stretching of the valve ring) in 10 Slight or late cyanosis was present in 31 cases Excessive pulsation of the lung hilum was noted by roentgen ray in 31 of the 50 cases so studied but a hilar dance was observed in only 5 Normal rhythm was the rule being present in 47 cases

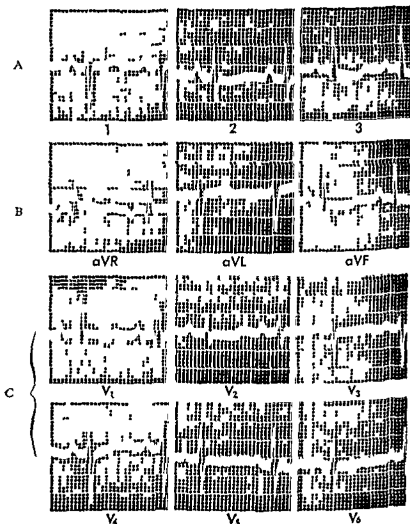


FIG 67 Electrocardiogram in a case of atrial septal defect female age 26 (A) Bipolar limb leads 1 2 and 3 (B) unipolar limb leads aVR aVL and aVF (C) six precordial leads V_1 to V inclusive Time = 0 04 and 0 20 second amplitude 1 mm = 0 10 mv

Right ventricular preponderance was present in the electrocardiogram in 41 cases and complete right bundle branch block in 5 others

When there is but one atrium life is generally much limited but some cases of remarkable longevity are on record with few symptoms or signs Cyanosis is the rule thrills and murmurs are infrequent and dyspnea is inconstant Of 5 cases with one atrium and two ventricles cited by Abbott one lived to the age of 31 years the mean duration of life was 6 years Of 9 cases with



FIG 68 Roentgenogram of thorax of case of congenital defect of the interatrial septum showing extreme degree of dilatation of the pulmonary artery and its branches right and left along with enlargement of the right ventricle Note the shadows of cross sections of arteries Small aorta (Kindness of Dr Hugo Roesler Temple University Philadelphia)

one atrium and one ventricle the oldest case was 16 years at death and the mean age was 3¼ years

A very interesting association is that of *mitral stenosis with a defect of the interatrial septum* (Abbott 1915 Lutembacher 1916) There is a combined effect of both lesions The left atrium tends to remain small and the right atrium becomes very large receiving as it does the extra blood from the left atrium as well as from the great veins There have been noted murmurs over the sternum or just to the left presystolic and systolic in time ascribed to the passage of blood through the septal defect but it is naturally difficult to differentiate such murmurs from those due to the mitral valve disease and

transmitted thither certainly the most common cause of the basal systolic murmur in such cases is dilatation of the pulmonary artery which is invariably present The congenital deficiency of the atrial septum has been given credit for relieving somewhat the burden imposed on the pulmonary circulation and right ventricle by marked mitral stenosis and thereby aiding the prolongation of life Remarkable cases of this combination of mitral stenosis and atrial septal defect are on record including that of a woman of 74 years of age who had passed successfully through eleven pregnancies and three abortions (Firket 1880) a woman of 61 years who had gone through seven pregnancies without heart failure (Lutembacher 1916) and two other cases aged 74 and 62 years respectively (Bonnabel 1906) However interatrial septal defects alone if large impose a serious burden on the right heart and pulmonary circulation and therefore it does not appear likely that they can aid much in relieving the heart or lungs in the presence of mitral stenosis except probably to prevent attacks of acute pulmonary edema which are an infrequent but distressing complication of tight mitral stenosis when the heart beats too rapidly

A large atrial septal defect is always to be suspected when there is the combination of a loud pulmonary systolic (not continuous) murmur, marked prominence of the pulmonary artery and lung hilus shadows and small aortic shadow by roentgen ray and pronounced right ventricular preponderance by electrocardiogram in a person in fairly good health save for a variable amount of dyspnea In differential diagnosis it may be said that the cor pulmonale due to pulmonary disease or endarteritis gives less right axis deviation and less lung hilus engorgement while mitral stenosis is of course attended by its characteristic diastolic murmur

Surgical correction of uncomplicated but important atrial septal defects is now on trial and has been successful in a few cases (Murray 1948) [3] Correction of the atrial septal defect was done by passing sutures through the anterior wall beginning to the right of the aorta and pulmonary artery to emerge posteriorly through an area between the superior vena cava and right pulmonary veins These sutures were tied together posteriorly drawn taut and tied down firmly thus compressing the anterior and posterior walls of the atria In one of the cases described the right atrium diminished to at least one half its size in two minutes the patient s condition was improved

Ventricular Septal Defects

Next in frequency after atrial septal defects come ventricular septal defects of which in Abbott s series there were 315 instances including localized openings isolated or complicated (274 cases) complete absence of the septum in the biloculate heart (14 cases) and in the triloculate heart with one ventricle and two atria (27 cases)

Localized ventricular septal defects are generally associated with other

[3] In March 1951 Murray (personal communication) stated that he had performed the operation of closure of an atrial septal defect in seven cases with considerable improvement in three some improvement in two and death in two

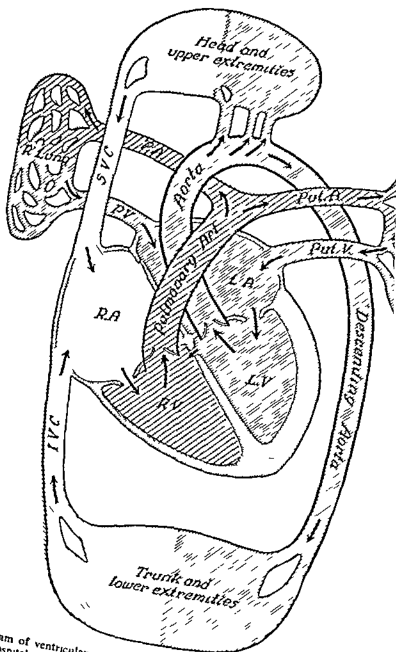


FIG 69 Diagram of ventricular septal defect (Kindness of Dr Helen Taussig Johns Hopkins Hospital Baltimore and The Commonwealth Fund New York City)

transmitted thither certainly the most common cause of the basal systolic murmur in such cases is dilatation of the pulmonary artery which is invariably present The congenital deficiency of the atrial septum has been given credit for relieving somewhat the burden imposed on the pulmonary circulation and right ventricle by marked mitral stenosis and thereby aiding the prolongation of life Remarkable cases of this combination of mitral stenosis and atrial septal defect are on record including that of a woman of 74 years of age who had passed successfully through eleven pregnancies and three abortions (Firket 1880) a woman of 61 years who had gone through seven pregnanc without heart failure (Lutembacher, 1916), and two other cases aged 74 a 62 years respectively (Bonnabel 1906) However interatrial septal defe alone if large impose a serious burden on the right heart and pulmona circulation and therefore it does not appear likely that they can aid much relieving the heart or lungs in the presence of mitral stenosis except probab to prevent attacks of acute pulmonary edema which are an infrequent b distressing complication of tight mitral stenosis when the heart beats t rapidly

A large atrial septal defect is always to be suspected when there is the com bination of a loud pulmonary systolic (not continuous) murmur mark prominence of the pulmonary artery and lung hilus shadows and small aort shadow by roentgen ray and pronounced right ventricular preponderance electrocardiogram in a person in fairly good health save for a variable amou of dyspnea In differential diagnosis it may be said that the cor pulmonale d to pulmonary disease or endarteritis gives less right axis deviation and le lung hilus engorgement while mitral stenosis is of course attended by characteristic diastolic murmur

Surgical correction of uncomplicated but important atrial septal defects now on trial and has been successful in a few cases (Murray 1948)[3] Corre tion of the atrial septal defect was done by passing sutures through the anteri wall beginning to the right of the aorta and pulmonary artery to emer posteriorly through an area between the superior vena cava and right pu monary veins These sutures were tied together posteriorly drawn taut an tied down firmly thus compressing the anterior and posterior walls of th atria In one of the cases described the right atrium diminished to at lea one half its size in two minutes the patient s condition was improved

Ventricular Septal Defects

Next in frequency after atrial septal defects come ventricular septal defect of which in Abbott s series there were 315 instances including localized oper ings isolated or complicated (274 cases) complete absence of the septu in the biloculate heart (14 cases) and in the triloculate heart with on ventricle and two atria (27 cases)

Localized ventricular septal defects are generally associated with othe

3 In March 1951 Murray (personal communication) stated that he had performed th operation of closure of an atrial septal defect in seven cases with considerable improvement i three some improvement in two and death in two

congenital defects and are almost invariably found at the base of the heart just below the aortic valve in the region of the so-called undefended or fibrous space Of the series of 274 cases collected by Abbott the ventricular septal defects were in this basal position in all but 17 and these 257 basal defects complicated other abnormalities in 207 cases leaving 50 instances of the pure defect. Seven of the 207 complicated cases had but a right sided (dextro-) position (Rechtslage) of the aorta as an additional defect, con stituting the Eisenmenger complex while 51 had pulmonary stenosis with aortic dextroposition in 32 constituting the tetralogy of Fallot These com plications are important in that they favor cyanosis the dextroposition of the aorta is especially significant in this respect The sexes are about equally represented in pure interventricular septal defects of Abbott s series of 50 cases 21 were male 26 were female and the sex of 3 was not stated

The *pure ventricular septal defect* is usually small and more or less cir- cular or oval 1 to 2 cm in diameter (Figures 69 and 70) Its septal edge is often thickened and fibrous and the endocardium of the right ventricular wall opposite the opening is also similarly affected probably by the repeated impact of the blood stream from the left ventricle The right ventricle is usually somewhat enlarged (hypertrophied and dilated) and the pulmonary artery is slightly dilated the left ventricle also may be bigger than normal The shunt through the uncomplicated septal defect is arteriovenous that is, left to right except under unusual conditions

There are no symptoms of pure ventricular septal defects unless they are very large and in rare cases there are no signs Usually however there is a loud blowing systolic murmur heard best just to the left of the midsternum and not widely transmitted When the murmur is very loud there is a palpable thrill also but this is occasionally absent Cardiac enlargement may or may not be evident on physical examination and by roentgen ray The electro- cardiogram is normal except in a few cases with abnormal right axis deviation and in rare cases in which the septal defect is associated with abnormality of the atrioventricular bundle (of His) with resulting congenital heart block. Cyanosis is rare in the case of uncomplicated ventricular septal defect and is practically only a terminal condition the shunt being reversed to become venoarterial or right to left when the right ventricular pressure exceeds that in the left ventricle in pneumonia or some other such complication Infre- quently when the septal defect is large the whole heart may be much increased in size and fail with characteristic congestive signs and symptoms including dyspnea

An isolated interventricular septal defect has been called *Roger s disease* (Roger 1879) and the murmur caused by this defect has been called *Roger s murmur*

Roger H "Recherches cliniques sur la communication congenitale des deux cœurs par inocclusion du septum interventriculaire" *Bull de l'Acad de med* 1879 2me ser VIII 1074

The following conclusions of this original publication are of interest (translation by myself)

1 There is a *developmental defect of the heart* from which cyanosis does not result in spite of the communication between the two ventricular cavities and in spite of the free mixture of venous blood with arterial blood This congenital abnormality which is compatible even with a long life is a simple one without the coexistence of congenital pulmonary stenosis It consists of a defect (opening) in the interventricular septum

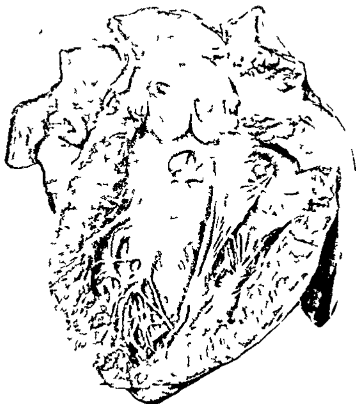


FIG 70 Photograph of the heart of a boy showing a congenital interventricular septal defect of small size just below the aortic valve The child had a typical loud systolic *murmur (Roger s murmur) with thrill at the left border of the sternum* maximal in *the third and fourth intercostal spaces*

"2 It is important to distinguish this cardiac anomaly which I have recently been the first to study clinically not only from other malformations but especially from acquired heart disease It is revealed only on auscultation by a physical sign with very special characters this is a long loud murmur (produced by the passage of blood through the interventricular opening and directly into the pulmonary artery or the aorta the site of which is frequently abnormal in these cases) This murmur is uncomplicated by other murmurs it begins with systole and is prolonged to such an extent that it entirely covers the natural tic tac of the normal heart sounds It has its maximum intensity neither at the apex (as in the case of

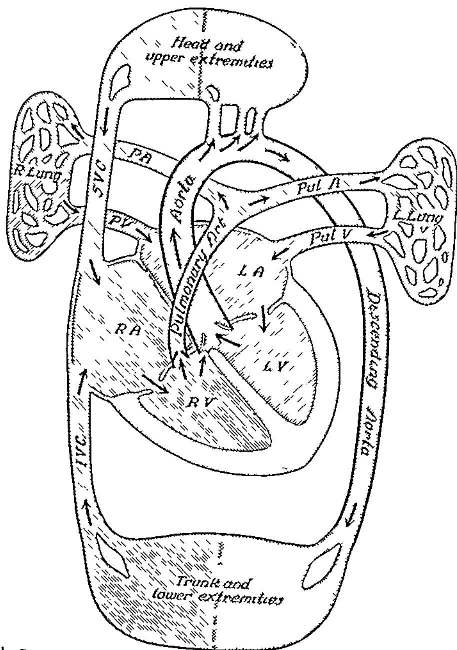


FIG 71 Diagram of tetralogy of Fallot (Kindness of Dr Helen Taussig Johns Hopkins Hospital Baltimore and The Commonwealth Fund New York City)

lesions of the auriculoventricular orifices) nor at the base to the right (as in aortic stenosis) nor to the left (as in pulmonary stenosis) but over the upper third of the precordial region It is chiefly median in position like the septum itself and from this central point it diminishes in intensity uniformly as one moves the stethoscope over the chest The murmur is not transmitted to the vessels It coincides with no other sign of organic disease except the *harsh thrill* which accompanies it This murmur is *the pathognomonic sign of an interventricular septal defect*

3 *The differential diagnosis* of this malformation (until now unrecognized or confused with other congenital or acquired lesions) will be henceforth rendered easy by attentive comparison of the physical signs These signs vary in number site and characteristics in heart disease when structural changes are multiple progressive and changing while the murmur in question like the permanent unchanging lesion causing it remains without modification for an indefinite time The same statement is true in comparing this murmur with signs of functional disorders such signs are very variable according to the diverse periods of cardiac weakness and they are totally dissimilar in their acute or chronic nature from the constant signs of defective interventricular septum which change hardly at all with the years and increase only very slowly and almost insensibly

4 The consideration of the age of the subject is a capital point in the diagnosis endocarditis for example shows itself almost never in infancy before the age of two years and on the other hand the anemia of very young children is almost never attended by a heart murmur The result is that a *murmur in a nursing infant* is almost a certain indication of an *anomaly* of the heart or great vessels

5 The *prognosis* is in general less grave in the malformation described above than in other organic diseases of the heart in which the danger for children is greater and nearer permitting hopes for scarcely more than another decade of life In spite of the presence of an uncomplicated interventricular septal defect individuals can reach and even surpass the average duration of human life

6 An exact diagnosis ordinarily demands in heart disease an active persistent *treatment* If on the other hand there is a congenital malformation of the heart *vigorous treatment is useless and even harmful To show thanks to precision in* diagnosis when to act in one case and when to refrain in another is to render a service not only to physicians but also to patients

It is of interest to note that Roger first described the condition and murmur that go by his name without having correlated in the same patients clinical and postmortem data He had made observations clinically and pathologically but not in the same cases Later however his deductions were confirmed

Although an interventricular septal defect is theoretically not a serious lesion it is a handicap which shortens life In Abbott s series of 50 pure cases the mean duration of life was only 14½ years, the oldest case being 49 years old One of the chief reasons for this shortening of life has certainly been in the past subacute bacterial endocarditis which Gelfman and Levine (1942) found to have complicated 57 per cent of 14 autopsied cases With prophylactic use of penicillin and of other new specific therapy against infections this situation will be radically changed and the prognosis will doubtless be *very much brighter especially since the septal defect itself causes*

relatively little strain on the heart Protection of such a patient is especially needed at the time of dental extraction when 300,000 units of penicillin should be injected intramuscularly 1 hour before the extraction and again 3 hours after to get rid of any alpha hemolytic streptococci that may get into the blood stream If subacute bacterial endocarditis is already present involving the edge of the defect in the right ventricle or the tricuspid valve or adjacent ventricular endocardium opposite the opening penicillin in large dosage (800 000 to 1,000 000 units a day) should be given for several weeks or if ineffective multiplied several times or supported or replaced by streptomycin For details of this therapy consult Chapter 15 Subacute Bacterial Endocarditis

Treatment of a pure isolated ventricular septal defect by surgery was hardly dreamed of when the first three editions of this book were published but now it is only a matter of time before such correction becomes a practical routine already animal experimentation has demonstrated its possibility and the first successful attempts have been made in man (Murray 1948)[4] The technic as described by Murray consisted of introducing a strip of fascia lata into the right ventricle and attaching it to the septum The details of this delicate operation are described by him in the Annals of Surgery, 1948 XXVIII 843

Still more important will some day be the prevention of this as well as other congenital cardiovascular anomalies by the prevention or early cure of diseases virus (like rubella) and otherwise that beset the mother during the critical stage of the fetal heart development in the first trimester of pregnancy

The tetralogy of Fallot This commonest of all combinations of congenital cardiac defects and one of the most serious has already been presented in part as an interesting and characteristic malformation in the early pages of this chapter (page 290 and Figure 64 page 299) but it belongs in the group of ventricular septal defect variations and so will be further discussed here (Figure 71) As noted above the four essentials of this relatively common anomaly are (1) a high ventricular septal defect (2) a dextroposed aorta overriding the septal defect (3) stenosis of the pulmonary valve or of the right ventricular infundibulum below it and (4) a much hypertrophied right ventricle It was encountered in 85 of Abbott s 1 000 autopsied cases of congenital defects of heart and great vessels There are always cyanosis and finger clubbing from earliest childhood often intense the cyanosis being increased by exercise which readily distinguishes it from the slaty blue color of argyria which is decreased when the skin flushes after exercise Shortness of breath a tendency frequently to squat weakness and faintness or even syncope are usual symptoms A moderate to loud pulmonary systolic murmur on auscultation blunt shoe shaped heart with prominent aorta and decreased pulmonary vascular shadow on x ray examination (Figure 72) and marked

4 By March 1951 Murray (personal communication) had operated to close ventricular septal defects in 13 cases with clear evidence of success in 7 (disappearance of murmur decrease of heart size abolition of shunt as shown by cardiac catheterization and increase of energy) 3 cases died

right ventricular preponderance by electrocardiogram (Figure 73) complete the diagnostic evidence Polycythemia and excessive hemoglobin even up to double the normal are in accord with the intensity of the cyanosis Cardiac catheterization quickly reveals the dextroposed aorta into which the catheter

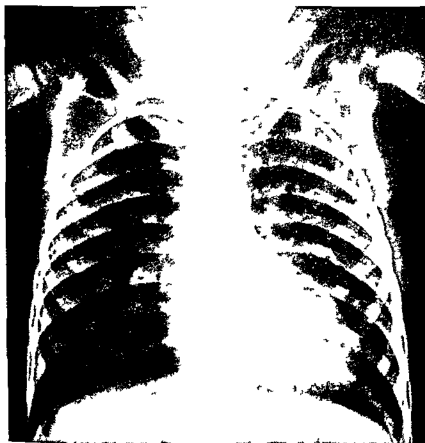


FIG 72 Roentgen film of the thorax in a case of tetralogy of Fallot

readily passes There may be the complication of patency of the ductus arteriosus with the tetralogy of Fallot and if so there is much less cyanosis There is in such cases a continuous murmur to the left of the sternum with the aorta in its ordinary position but with a right sided aorta the murmur is to the right of the upper sternum

The prognosis of the tetralogy of Fallot is generally bad for a long life the average duration in Abbott s series of 85 cases being 12 years but a few patients reach middle age and one established the record of 59 years and 8 months (White and Sprague 1929) Fatal complications include cerebral abscess cerebral thrombosis bacterial endocarditis respiratory infections and right heart failure

The treatment was stated in the first three editions of this book to be only ordinary common sense protection of a cardiac cripple but in the few years that have elapsed since then a great advance has been recorded Blalock and Taussig in 1945 introduced a surgical operation that has greatly ameliorated the symptoms and signs of the disease although they have not cured it The

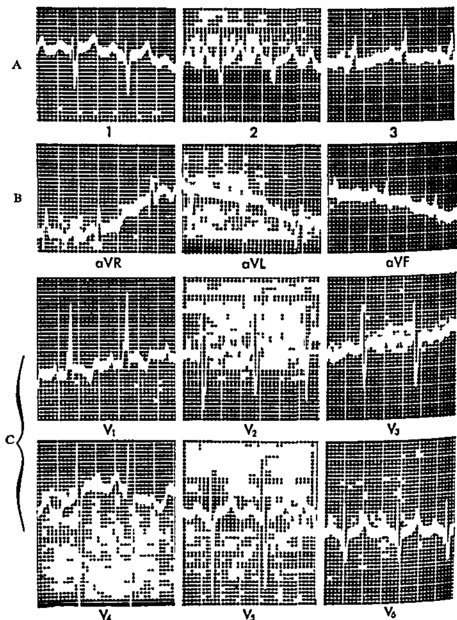


FIG 73 Electrocardiogram in a case of tetralogy of Fallot male age 3 (*A*) Bipolar limb leads 1 2 and 3 (*B*) unipolar limb leads aVR aVL, and aVF (*C*) six precordial leads V to V inclusive Time = 0 04 and 0 20 second amplitude 1 mm = 0 10 mv

procedure consists of the anastomosis of the right or left subclavian artery or in a few instances of the innominate artery to one of the pulmonary arteries thereby bringing blue blood into the lungs for oxygenation largely if not wholly relieving the cyanosis dyspnea weakness polycythemia and clubbing of the fingers in a most dramatic way At the time of writing 1 045 cases of the morbus caeruleus mostly consisting of the tetralogy of Fallot or some variation thereof had been subjected to this operation in Blalock s clinic with a mortality of approximately 18 per cent and a high degree of improvement in the majority of the survivors (Blalock personal communication 1951)

Another technic to aid the victims of the tetralogy of Fallot in a similarly effective way has been introduced by Potts (1946) and consists of a somewhat simpler procedure of side to side anastomosis of aorta and pulmonary artery This operation of Potts has one particular advantage over that of Blalock in that it may be easily carried out in very young infants who might readily expire as a result of the tetralogy of Fallot before they reach the age in which Blacock s anastomotic operation is feasible In both types of operation however it should be noted that a new defect has been introduced by the surgical procedure amounting essentially to a left to right shunt which acts like an arteriovenous communication to increase the work of the heart Taussig (1948) has demonstrated by x ray the increase in heart size that follows the operation even while great improvement is shown by the child Also a continuous murmur resembling that of a patent ductus arteriosus results from the operation Despite this unfavorable point the life of these children has undoubtedly been prolonged though just how much it is still impossible to say The most suitable age for either of these two surgical procedures is probably between 6 and 18 although successful results have been noted earlier and later A more recent surgical procedure has been introduced by Brock (1948) and consists of valvulotomy of the stenosed pulmonary valve the clearing of cyanosis has been noted in a few cases but it is still too early to evaluate this therapy

An important though not very common complication of the tetralogy of Fallot is subacute bacterial endocarditis and therefore the same advice about the therapeutic and prophylactic use of penicillin given for a localized pure ventricular septal defect (see above) should apply here

Finally as stated in the general discussion of congenital heart disease the most important consideration of all is that of the prevention of such a malformation as the tetralogy of Fallot This will doubtless depend in large measure on the protection of the mother from various deleterious influences including virus infections (such as rubella) during the first three months of pregnancy

The Eisenmenger complex Another but much rarer variation of the group of ventricular septal defects is that described by Eisenmenger (1897) consisting of this defect overridden by a dextroposed aorta and accompanied by a large right ventricle but with no pulmonary stenosis There were only 7 such cases in Abbott s series of 1 000 in contrast to the 85 patients with the

tetralogy of Fallot The symptoms and signs are much the same however in the two conditions though generally less pronounced in the case of the Eisenmenger complex which lacks the loud pulmonary systolic murmur and which also shows a normal or even somewhat prominent pulmonary vascular tree on x ray examination

The prognosis with this complex is still not good but in Abbott s series was far better than that of Fallot s tetralogy the mean age being 25 years as contrasted with 12 years On the other hand there is as yet no surgical correction here because a considerable amount of blood does go to the lungs the difficulty consists in the equally large amount of blue blood that enters directly into the systemic circulation

Entire absence of the ventricular septum so that the heart is **three chambered (cor triloculare biatriatum)** or **two chambered (cor biloculare)** is rare Surprisingly efficient circulation is possible even with such marked deformity and cases surviving to adult life are on record Although in these cases there is but one ventricle the course of the two blood streams entering it from the atria is often so directed in relation to their inflow and outflow tracts that they may actually mix but relatively little and so not conduce to much of any cyanosis or immediately serious disability of the circulation In Abbott s series of 5 cases with one ventricle and two atria one lived to be 31 years old and the mean age was 6 years There are usually no murmurs or thrills in such cases the cyanosis may be but slight or even absent and the heart may be but little enlarged rendering the diagnosis difficult or impossible The cor biloculare occurred in 9 of the 1 000 cases of Abbott s series, the mean age at death was 3¼ years and the oldest case lived to be only 16

To be distinguished from a congenital interventricular septal defect there occurs rarely a septal defect due to inflammatory ulceration through the upper septum in bacterial endocarditis or following coronary thrombosis Such a lesion is relatively small and usually of little importance as a complication of fatal bacterial endocarditis but it is a factor of added and serious and usually fatal strain in acute myocardial infarction

An interesting and important rare complication of an interventricular septal defect is **congenital heart block** which has never been found without this structural lesion in itself it is not serious and is apparently compatible with a long life and full activity (Campbell 1943) (see Chapter 34)

Anomalous papillary muscles and chordae tendineae In rare hearts there exist unimportant anomalies of the papillary muscles and chordae tendineae for example a papillary muscle found attached to the pulmonary valve in the routine autopsy of a man 69 years old (Collins 1931) and a chorda tendinea extending across the left ventricular cavity from a small papillary muscle of its own to be attached well up on the aortic cusp of the mitral valve in a man of 40 years (Hamilton and Byers 1899) The only importance of such cases lies in the occasional occurrence of unusual snapping intrasystolic sounds or twanging systolic murmurs which may cause undue apprehension

CONGENITAL MYOCARDIAL DISEASE

The heart muscle may be involved congenitally in a variety of ways The most common change is that of **hypertrophy,** with or without dilatation secondary to various valvular septal and vascular defects (for example pul monary stenosis large interatrial septal defect coarctation of aorta) This response to increased work and strain is comparable to that found in acquired valvular heart disease and chronic hyperpiesia The muscle fibers are hypertrophied in whatever heart chambers are under particular strain the right ventricle being by far the most commonly affected compared with the situation a decade or two ago There are now but few cases of enlargement of this sort that are unexplained these are grouped as congenital idiopathic hypertrophy There have been slowly separated from this group three other myocardial changes that are of importance One consists of **necrosis and fibrosis** associated with hypertrophy explained on the basis of (1) infection and (2) anoxia and most clearly evident in instances of very faulty anomalous blood supply as for example when the left coronary artery arises from the pulmonary artery A second myocardial change is that of the deposition of glycogen in large amounts in vacuoles in the heart muscle in the so called **glycogen storage disease (von Gierke's disease,** von Gierke 1929 Pompe 1933) here the enlargement and glycogenization of the heart (Figure 74) are but part of the systemic disease of faulty glycogen metabolism with similar involvement of other organs in the body (especially the liver) fasting hypoglycemia failure of hyperglycemic reaction readily elicited ketosis and ketonuria and early death The third myocardial condition recently recognized is the dilatation with secondary hypertrophy occurring in very young infants due to **excessively fast heart rates in paroxysmal tachycardia** (Hubbard 1941) (see Chapter 32)

Congenital idiopathic hypertrophy of the heart One of the least common congenital anomalies of the heart is that which has been called idiopathic hypertrophy The actual number of cases of congenital idiopathic hyper trophy has been steadily shrinking in recent years because of the special studies which have separated from it the rare cases of glycogen storage disease (von Gierke s disease—see above) myocarditis apparently of infectious origin (Kugel and Stoloff 1933) instances of extensive myocardial necrosis with fibrosis such as that occasioned by a very abnormal coronary blood supply (Bland White and Garland 1933) and cardiac enlargement secondary to formerly unrecognized paroxysmal tachycardia of excessively fast rates in infancy (see above and Chapter 32) There still remain a few unexplained cases

The heart in congenital hypertrophy (idiopathic or not) is frequently two or three times the normal weight (75 gm for example instead of 25 gm at the age of 4 months) and may also be considerably dilated In one of our own cases found to be due to glycogen storage disease the heart weight was five

times the normal 175 gm instead of 34 (Figure 74) The cardiac enlargement is easily made out on physical examination and by roentgen ray The heart shadow is uniformly enlarged and roundish in shape prominent to right of the midline as well as to left and without particular dilatation of the atria or great vessels (arteries or veins) The electrocardiogram in uncomplicated cases is not remarkable but with coronary anomalies it may be very abnormal (see end of this chapter)

The male sex is more frequently involved than the female The course is

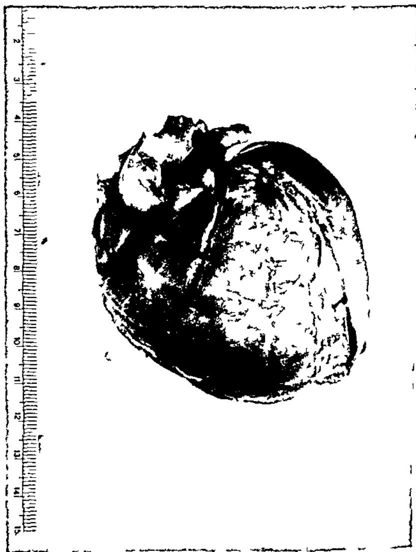


FIG 74 Congenital hypertrophy of the heart due to glycogen storage (von Gierke's) disease This heart of a 7 month-old infant weighed 175 gm instead of the average normal of 34 gm for this age Both ventricles were enlarged but the shape of the heart was not significantly altered from the normal

progressively a downhill one with symptoms and signs of circulatory embarrassment and weakness during the first year of life Death comes rather suddenly or after increasing dyspnea or systemic venous congestion at about six months to a year or two of age the oldest patient of Abbott s series of 10 lived only four years

There is no treatment as yet but further study will doubtless reduce still more the number of cases of congenital idiopathic hypertrophy that are wholly unexplained

CONGENITAL ENDOCARDITIS AND VALVULAR DEFECTS

Although acute endocarditis has been noted in the fetus and in the infant at birth it is the late result of such inflammation that is much more frequently seen and which doubtless explains some congenital cardiac defects Occasionally in cases with pulmonary stenosis aortic stenosis and other congenital valvular lesions and rarely even in hearts without such lesions the endocardium lining a part or the whole of a heart chamber may be thick and white due to marked fibrosis the only adequate explanations of which are in most cases a state of chronic anoxia or strain or a fetal endocarditis the deformed valves in such cases are also thickened and scarred as a rule

Any heart valve or chamber may show this abnormality but the pulmonary valve and the infundibulum of the right ventricle are much more commonly involved than any other part of the heart quite probably because of the fact that they bear the brunt of the chief cardiac circulatory effort in fetal life, the aortic valve comes a very late second while the mitral and tricuspid valves are affected only rarely In Abbott s series of 1 000 cases there were 150 cases of pulmonary or infundibular stenosis or atresia 35 cases of aortic or subaortic stenosis or atresia 19 cases of tricuspid stenosis or atresia and but 11 cases of mitral stenosis or atresia Only rarely except in the cases with aortic valve involvement were the valvular defects uncomplicated the reason for the relatively common uncomplicated occurrence of aortic or subaortic stenosis is probably its late development in the course of intrauterine life Preponderant valvular regurgitation of congenital origin (involving the tricuspid pulmonary or aortic valve) is excessively rare as is also multiple valvular disease Rheumatic valvular disease may infrequently be found as a complication of congenital heart disease

Pulmonary valve or infundibular stenosis is in the vast majority of cases complicated by septal defects (101 of 110 cases in Abbott s series) most commonly ventricular alone (51 of Abbott s cases) less often both atrial and ventricular (34 of Abbott s cases) and rarely atrial alone (16 of Abbott s cases) Quite often it is associated not only with a ventricular septal defect but also with dextroposition of the aorta and marked right ventricular enlargement to form the tetralogy of Fallot (see page 318) The signs course and prognosis vary greatly according to the degree of the pulmonary valve or infundibular stenosis and of the associated anomalies particularly the degree

of aortic dextroposition When pulmonary stenosis is a part of the tetralogy of Fallot cyanosis is invariably present with an atrial septal defect cyanosis *and finger clubbing are less than in the case of the tetralogy* of Fallot but when pulmonary stenosis is independent of septal defects which is a much rarer situation cyanosis is not present until the right heart fails on which occasion stasis in the peripheral circulation is the explanation The characteristic sign of pure pulmonary stenosis is a loud pulmonary systolic murmur with accompanying thrill Congenital pulmonary stenosis has itself in recent years been relieved surgically in a considerable number of cases Valvulotomy was introduced by Brock in 1948 Blalock has followed suit and reports (personal communication 1951) having operated upon 42 cases of valvular pulmonary stenosis with intact ventricular septum with 8 deaths

Congenital pulmonary regurgitation is very rare (see Chapter 26 for signs of this valve defect) it may complicate pulmonary or infundibular stenosis **Pulmonary valve atresia** (closure) is always attended by other compensatory anomalies it allows but a very few years of life as a rule, the mean age in Abbott s 40 cases being 4 years and the oldest 30 years

Aortic valve or subaortic stenosis is one of the rarer congenital anomalies It doubtless is sometimes wrongly diagnosed as acquired aortic stenosis the signs and course of both are outlined in Chapter 26 The valve is no more frequently involved (11 cases of Abbott s series) than the infundibulum of the left ventricle just below the valve (subaortic stenosis) (12 cases of Abbott s series) **Congenital aortic regurgitation** of any high degree has not yet been reported so far as I am aware in slight degree it may complicate aortic stenosis or the dilatation of the aorta encountered in the tetralogy of Fallot **Aortic valve atresia** is incompatible with life for more than a few months at best (maximal age of the 12 cases of Abbott s series 15 weeks mean age 8 weeks) there must of necessity be a compensatory patency of the ductus arteriosus

Mitral and tricuspid valve stenosis and atresia are rare anomalies almost always attended by compensatory septal defects The average duration of life in cases with these anomalies is short The commonest of these defects is tricuspid atresia of which there were 16 examples in Abbott s series the oldest survived to the age of 56 years There were 3 cases of tricuspid stenosis (the oldest 28 years of age) 6 cases of mitral stenosis (oldest 27 years), and 5 of mitral atresia (oldest 3½ years) Clinical recognition of defective development of the right ventricle associated with tricuspid atresia or hypoplasia has been established (Taussig 1936) the diagnostic criteria consist of cyanosis in infancy much diminished roentgen ray shadows of right ventricle and pulmonary artery left axis deviation by electrocardiogram (Figure 75) and absence of murmurs It is to be treated surgically by Blalock s or by Potts operation as in the case of the tetralogy of Fallot (q v for details) In very young infants Potts operation is more suitable than Blalock s and may be lifesaving prior to the time of the arrival at the age when the more complicated procedure is feasible (Gasul et al 1949) **Tricuspid regurgitation**

has been described and is due to displacement of the attachment of the cusps of the valve (Ebstein 1866 Yater and Shapiro 1937)

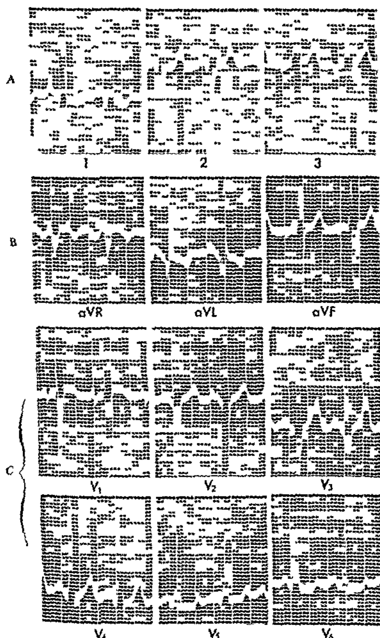


FIG 75 Electrocardiogram in a case of tricuspid atresia male age 7 years (*A*) Bipolar limb leads 1 2 and 3 (*B*) unipolar limb leads aVR aVL and aVF (*C*) six precordial leads V to V inclusive Time = 0 04 and 0 20 second amplitude 1 mm = 0 10 mv

CONGENITAL PERICARDIAL DEFECTS

There are several types of pericardial abnormality of congenital origin all rare These include absence or defects of the parietal pericardium (30 cases in Abbott s series), and diverticulum or hernia (6 cases in Abbott s series)

The parietal pericardium may be entirely absent so that the heart lies in the left pleural cavity along with the left lung or it may be defective in part most commonly over the region of the pulmonary artery In the case of ectopia cordis there may or may not be a pericardial sac the cases with better prognosis have such a sac When the parietal pericardium is absent the heart is usually freely movable both on respiratory movements and with changes of body position physical examination and especially roentgen ray study may reveal this extreme mobility The clinical significance of absence or defect of the parietal pericardium is practically nil in itself normal duration and activity of life being possible without any cardiac strain or circulatory embarrassment Two complications may arise however One is due to close contact of heart with left lung and pleura so that disease of the latter may seriously affect the former and vice versa there no longer being protection by an intervening cavity Pleurisy with effusion empyema and pneumonia have been reported as fatal illnesses in the cases on record with absence or deficiency of pericardium Another complication of importance that has been reported resulting in pain or even death is sudden kinking of the great vessels due to the fact that the heart is so freely movable

The other two congenital anomalies of the pericardium diverticulum and absence of attachment are very rare and of no clinical importance when they do occur except that occlusion of the orifice and consequently distension of the cavity of a pericardial diverticulum may interfere somewhat with the heart s action

CONGENITAL ANOMALIES OF THE AORTA

Congenital aortic anomalies found mostly in young persons are due to maldevelopment in fetal life or at birth and include hypoplasia coarctation right aortic arch double aortic arch aneurysms and transposition of th aorta and pulmonary artery as well as septal defects between aorta and pulmonary artery right ventricle or auricle and patency of the ductus arteriosus

Aortic Hypoplasia

Hypoplasia (ὑπο under and πλασις formation) or small caliber of the aorta throughout its course is one of the commonest of the congenital aortic anomalies but in high degree it is relatively rare and it is then usually associated with other congenital cardiovascular defects In Abbott s series it was found in

77 cases 75 of which showed other defects the commonest associated abnormality was an atrial septal defect With such a defect there is a combination of a very large pulmonary artery and a small aorta due to the overloading of the pulmonary circulation and the underloading of the systemic There is general hypoplasia of the arterial system when there is much aortic hypoplasia with a tendency to pallor slow and incomplete growth and retardation of sexual development Small heart size and large heart size have both been reported in this condition and heart failure in youth is said to have resulted from the strain due perhaps in part to a high degree of aortic narrowness but more probably to complicating congenital defects in the heart itself

Coarctation of the Aorta

Coarctation (*co-* together and *arctare* to press or make tight) of the aorta is a localized narrowing of the aorta of greater or lesser degree in the vicinity of the insertion of the ductus arteriosus which sometimes remains patent Morgagni (1761) was the first to record its discovery at autopsy It is a fairly common abnormality having been noted in 142 of Abbott s series of 1 000 cases of congenital cardiovascular defects in 79 of which it was the primary lesion and in the other 63 a complication of other anomalies slight grades are likely to be missed even on postmortem examination and are of no clinical importance

Etiology and pathology There have been described two chief types of aortic coarctation called the infantile and the adult but there is not always a sharp separation between them The first (or infantile) a rare type (37 cases in Abbott s series only 9 of which were primary) consists of narrowing of the whole isthmus that is that part of the aorta between the left subclavian artery and the ductus arteriosus sometimes the proximal arch itself is also involved In fetal life the isthmus has little function since blood enters the descending aorta largely through the ductus arteriosus therefore it quite naturally remains hypoplastic This fetal condition may persist for a few weeks or months after birth to a greater or lesser degree but rarely is it found in adult life In extreme cases it may be represented simply by a fibrous cord the circulation to the lower part of the body being taken care of wholly in such cases by the patent ductus arteriosus which thus supplies only venous blood to the abdominal viscera and legs with resulting disability The infantile type is serious usually associated with other important anomalies and had been thought to be incompatible with long life there having been a maximum of 9 months and a mean of 8 hours in Abbott s series of 9 primary cases However recently Johnson and Kirby (1948) have reported using in three patients aged 13 17 and 20 years respectively the left subclavian artery to bridge the long gap of the coarcted aorta of the infantile type with success in one case partial benefit in a second and failure in a third

The second (or adult) type of aortic coarctation consists of localized constriction of the aorta at or most often just below the insertion of the ductus

arteriosus and rarely above that point (Figure 76) It is much more common than the infantile type and less serious in Abbott s series there were 105 cases in only 35 of which the condition complicated other defects It is probably always a prenatal condition developing in the fetus In only a few of the cases does the ductus arteriosus remain patent There may be other congenital cardiovascular anomalies especially when the coarctation is extreme

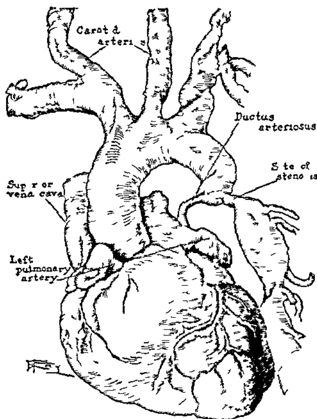


FIG 76 Coarctation of the aorta (adult type) just below the ligamentum arteriosum (Case of Dr W D Shelden) (Blackford Coarctation of the Aorta *Arch Int Med* May 1928)

but frequently the condition is uncomplicated The most common associated anomaly is the bicuspid aortic valve either congenital or acquired in origin found by Abbott in 50 out of 183 collected cases (Abbott 1928) and in 4 per cent of 104 additional autopsied cases reported by Reifenstein et al in 1947 All grades of narrowing of the aorta occur from that which is so slight that it can scarcely be seen on careful postmortem scrutiny up to complete local aortic obliteration Coarctation has been noted more often in the male than in the female the adult type being three to five times more frequent in the male sex why this is so is not known In a recent series of 96 cases reported at the Mayo Clinic (Christensen and Hines 1948) there were 76

males and 20 females this ratio is characteristic of other series It has also been found in more than one member of a certain family (Walker 1934)

The result of pronounced coarctation of the aorta of the adult type on the circulation is of much interest The aorta is usually considerably dilated above the constriction (sometimes with an aneurysm) and often but not always narrowed below A collateral circulation is developed at times in high degree blood being carried to the lower part of the body by widely dilated tortuous internal mammary scapular and intercostal arteries The heart becomes enlarged in most cases and sometimes is markedly hypertrophied and dilated Hypertension accompanying the coarctation is responsible for this cardiac hypertrophy as a rule but on occasion acquired valvular disease which is a not infrequent complication may be an additional factor The arterioles in the muscle and skin of the arms in young subjects are normal and indistinguishable from those in the legs (Graybiel Allen and White 1935) The hypertension usually found in persons with aortic coarctation need not be wholly ascribed to the defect directly but may be due in part at least to a secondary effect namely the diminution of the renal blood flow below the constriction which in turn causes a generalized vasoconstriction reflexly or through the production of the chemical mediator called hypertensin or angiotonin (see Chapter 19) (Steele and Cohn 1938) when the collateral circulation is very richly developed the blood pressure may be perfectly normal the renal circulation also then being adequate The early hypertension in cases of aortic coarctation is sometimes attended by congenital intracranial aneurysms (as in the circle of Willis) Also unusual blood supply to the teeth has been reported in coarctation of the aorta

Symptoms and signs There are no particular symptoms of the adult type of coarctation of the aorta and often no signs or so slight that the anomaly escapes notice during life With high grades of coarctation however there are a number of important signs (1) inequality of blood pressure and of pulse fullness and form between the upper and lower extremities the brachial systolic pressure often being much elevated (even to 200 mm of mercury or more) while the femoral blood pressure is low (100 mm or less as a rule) and the femoral pulse is small although the diastolic pressure levels may be much the same (2) evidence of compensatory collateral circulation between the upper and lower parts of the body the internal mammary intercostal scapular and deep epigastric arteries being much dilated tortuous and in the case of the first three groups of vessels easily felt and sometimes visibly pulsating (3) long systolic murmurs transmitted from the aortic coarctation itself heard not only over the precordium and back but especially down the spine where it may be heard to extend into diastole and also along the course of the dilated tortuous anastomotic vessels sometimes accompanied by palpable thrills (4) decrease or absence of the shadow of the aortic knob by roentgen ray frequently with dilatation of the ascending aorta and first part of the arch (5) roentgen ray evidence of well marked notching of the ribs due to the dilated tortuous intercostal arteries (Figure 77) and (6) enlargement of

the heart and sometimes signs of failure due in part to frequent complicating heart lesions (especially acquired valvular disease) but in large part to the hypertension associated with the stenosis of the aorta It should be reiterated that the brachial systolic pressure is not always high in cases of coarctation of the aorta but there is almost always a greater blood pressure in arms than in legs Retrograde arterial or direct aortic Diodrast injections can helpfully outline the roentgen ray shadow of the coarcted aorta and of some of the collateral circulation for confirmation of the diagnosis and especially as guidance for the surgeon

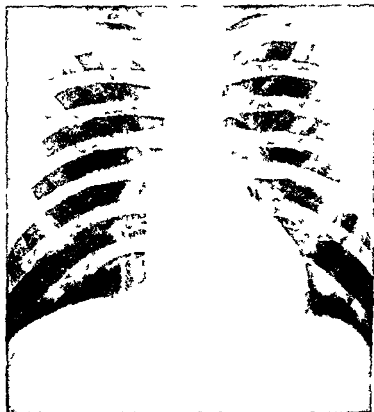


FIG 77 X ray photograph of a 19 year-old boy with coarctation of the aorta demonstrating notching of the ribs and absence of aortic knob (Blood pressure in the arms 175/110 blood pressure in the legs 135/100)

Course and prognosis Complications The course and prognosis of coarctation of the aorta vary enormously depending chiefly on the degree of narrowing of the aorta and the extent of the collateral circulation but even when slight the condition is important because of the possibility of local infection in the form of subacute bacterial aortitis or endocarditis of a bicuspid aortic valve Marked coarctation is often a serious anomaly which may kill in youth by one of four complications heart failure rupture of the aorta itself apo-

plexy due to cerebral hemorrhage or thrombosis and bacterial infection in vading the area of coarctation or the aortic valve On the other hand it is compatible with long life as in the case of a 92 year old man with completely closed aorta (Abbott 1928)

Of a series of 200 cases of the adult type collected by Abbott (1928) the average age at death was close to 32 years with extremes of 3 and 92 years 60 died of congestive heart failure 40 of sudden heart (2) or aortic (38) rupture 26 of cerebral complications and 14 of bacterial endarteritis Of a more recent series of 104 autopsied cases (Reifenstein et al 1947) 23 per cent died of rupture of the aorta 22 per cent of bacterial invasion 18 per cent of congestive heart failure 11 per cent of intracranial lesions and 26 per cent of incidental causes

Between 5 and 10 per cent of cases with coarctation of the aorta have an associated patency of the ductus arteriosus for example 8 of 140 cases sur gically treated by Gross (personal communication 1950) 10 per cent of a series at the Mayo Clinic (Taylor et al 1950) and 10 per cent of Abbott s cases

Treatment In the last edition of this book it was stated that there was no special therapy for congenital coarctation of the aorta but that the subject should be protected as much as possible from physical strain and infections In the intervening years there has occurred a great advance due to the intro duction independently by Crafoord (1945) and Gross (1945) of surgical correction of the defect by excision of the area of coarctation and end to end anastomosis of the cut ends of the aorta in children and young adults where the narrowed portion is long the left subclavian artery or a vascular graft can be used to bridge the gap Postoperatively the blood pressures in arms and legs equalize at normal levels Of the first 100 cases operated upon by Gross (1950) 11 died and they were for the most part early cases of the others 71 were completely relieved 8 others satisfactorily improved one unchanged and 9 explored only (because of findings contraindicating operations on the aorta itself) Blalock has written to me (February 1951) of having operated upon 103 cases of coarctation of the aorta with 11 deaths

Differential diagnosis There is one condition with which coarctation of the aorta is commonly confused and that is hyperpiesia (essential hypertension) The differentiation is however easy if one has in mind the possibility of the congenital defect especially in a child or young adult the difference between the blood pressures of arms and legs the systolic or continuous murmur trans mitted down the upper spine the palpable intercostal artery pulsations and the notching of the ribs seen by roentgen ray at once lead to the correct diagnosis

Other Rare Congenital Aortic Anomalies

These are (1) localized weakness of the wall resulting in aneurysms usually small (2) transposition of the aorta and pulmonary artery so that the former

arises from the right ventricle and the latter from the left as the result of reversed torsion of the common arterial trunk in the course of fetal development (3) a right sided instead of a normal left sided aortic arch and (4) a double aortic arch due to persistence of the right hand side of the fourth primitive arch

Congenital defects in the aortic wall Congenital defects in the aortic wall with thinning and even outpocketing (aneurysm) are very rare and small They are an incidental finding at postmortem examination and are of no clinical importance The medial necrosis responsible for dissecting aneurysms does not belong here

Transposition of the great arteries Transposition of the great arteries is an infrequent anomaly found much more often in the male sex than in the female in the ratio of about 4 to 1 It is incompatible with survival for more than a few hours or days after birth unless there is a septal defect which allows some venous blood to reach the lungs such defect usually consists of a patent foramen ovale In some cases there is also an interventricular septal defect or a patent ductus arteriosus When the ventricular septum is defective life may last for years but the handicap is a serious one and death occurs almost always before adult age is reached and is due to heart failure or complicating infections In Abbott s series of 1 000 cases of congenital cardiovascular defects there were 74 cases of complete transposition of the aorta and pulmonary artery in 49 of which it was the primary defect Of these 49 cases, 32 had a closed ventricular septum with longest survival to 11 years while 17 had a ventricular septal defect with longest survival to 16 years

Cyanosis is an almost invariable sign of complete transposition of aorta and pulmonary artery except in early infancy when the cyanosis tends to be absent or less marked than later as is the case also in some other congenital cardiac anomalies the cyanosis sometimes becomes very marked and it is then accompanied by definite clubbing of the fingers The heart is enlarged particularly the right ventricle and the electrocardiogram shows abnormal right axis deviation Roentgenologic study may show little except the cardiac enlargement but there may be some suggestion of the anomaly of the great arteries especially in the oblique views There may or may not be heart murmurs and thrills dependent on the presence of other anomalies such as patency of the ductus arteriosus uncomplicated transposition of the great arteries should not cause murmurs

The antemortem diagnosis of complete transposition of the aorta and pulmonary artery is extremely difficult but Taussig (1938) has pointed out the combination of four characteristic features (1) persistent cyanosis (2) cardiac enlargement especially of the right ventricle (3) a narrow aortic shadow *in the anteroposterior roentgenogram and (4) an increase in the* width of the roentgenographic shadow cast by the great vessels when the patient is placed in the left anterior oblique position

A hopeful development in these very serious cases has taken place since the last edition of this book was published through the introduction by

Blalock of the production of an atrial septal defect and sometimes in addition the anastomotic operation which he has used in cases of the tetralogy of Fallot namely joining subclavian and pulmonary arteries on the right He has operated upon 62 cases with 38 deaths the best results have been in patients with pulmonic stenosis as well as transposition and in patients with the Taussig Bing syndrome (Blalock personal communication 1951)

Corrected transposition of the great vessels There is a condition called corrected transposition of the great vessels in which the aorta and pulmonary artery although in abnormal position regarding each other arise nevertheless from the correct ventricles Such an anomaly in slight degree is of little or no clinical importance since the circulation is maintained practically in a normal manner and the condition may not be very obvious even at postmortem examination When of marked degree however it is associated with other anomalies such as interventricular septal defects and life does not last beyond early adult years there were but 6 cases in Abbott s series 4 of which were primary in type with longest survival to 24 years

Finally a third type of transposition occurs called **partial transposition** in which both aorta and pulmonary artery arise from the same ventricle As in the case of complete transposition with septal defect there is frequently cyanosis Life is usually short in this condition averaging 4½ years in 16 primary cases collected by Abbott

Right or double arch Vascular ring Anomalies of the aortic arch consisting of a right or double arch are rare and for the most part unimportant except that there tends to be more or less compression of esophagus and trachea between the aorta and ductus arteriosus in the case of the right aortic arch and between the two sides of the arch when it is double In some cases this obstruction is an important complication and rarely it may be serious with *dysphagia* (called *lusoria* from the Latin meaning deceitful) esophageal dilatation and ulceration tracheal stenosis and asphyxia With obstruction of high degree and the diagnosis of right or double aortic arch established surgical cure by transecting the constricting vascular ring has been effected by Gross (1945) since the last edition of this book was published Dysphagia lusoria has also been noted in cases with certain other anomalies of the great arteries for example when the right subclavian comes off the descending thoracic aorta instead of the innominate artery The diagnosis must rest in the main at least on roentgen ray evidence of reversed position of the aortic arch or of its double character and on abnormal deviation or obstruction of the trachea and also of the esophagus as studied fluoroscopically during the ingestion of barium (Figure 78)

In Abbott s series there were but 5 cases of double aortic arch the oldest surviving to 87 years and 35 cases of right aortic arch 14 classified as primary with the oldest case 61 years females outnumbered males (8 to 5) in a small series of 13 cases of these two anomalies Abbott recorded 7 cases in her total collection of 1 000 who showed the right subclavian artery arising from the descending aorta and 8 cases with left subclavian artery arising

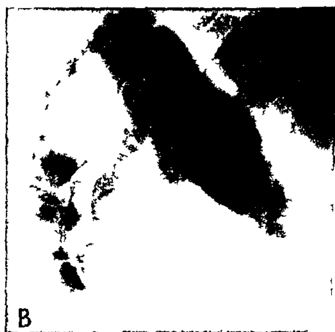


FIG 78 Roentgenograms showing a right aortic arch displacing trachea and barium filled esophagus forward and to the left (*A*) Anteroposterior view (*B*) right anterior oblique view (Kindness of Dr Hugo Roesler Temple University Philadelphia)

FIG. 79. Diagram of patent ductus arteriosus. (Kindness of Dr. Helen Taussig, Johns Hopkins Hospital, Baltimore, and The Commonwealth Fund, New York City.)

from either the ductus arteriosus or the pulmonary artery in the former group one of 5 cases lived to be 44 the oldest age noted while the one case of the latter whose age at death was noted was only 5 years old

COMMUNICATIONS BETWEEN THE AORTA AND PULMONARY ARTERY

There are four types of congenital communication between the aorta on the one hand and pulmonary artery right ventricle or right atrium on the other hand They are first and most common patency of the ductus arteriosus second rare cases of a persistent truncus arteriosus without separation into aorta and pulmonary artery third very rare instances of communication between the aorta and pulmonary artery by arterial septal defect and fourth very rare cases of communication between aorta and right ventricle or right atrium by septal defects The possible rupture of the aorta into right ventricle or right atrium in bacterial endocarditis and endarteritis or into the pulmonary artery in syphilitic aortitis is discussed elsewhere (see Chapters 15 and 28 respectively)

Patency of the Ductus Arteriosus

The ductus arteriosus (also called *ductus Botalli* Botallo 1530) which normally in the fetus diverts most of the blood from the pulmonary artery into the aorta should cease to function soon after birth it should be converted within a few weeks into a fibrous cord the *ligamentum arteriosum* Its obliteration may however be delayed for some months or it may persist as a patent arterial canal throughout life Its patency may be regarded as a con genital anomaly if it is found later than three months after birth (Figure 79) It is one of the commonest of all congenital cardiovascular defects ranking third in incidence (242 cases 92 as the primary and 150 as a complicating defect) after interatrial and interventricular septal defects respectively in Abbott s series of 1 000 cases Because of its curability now in childhood physicians in general have become much more familiar with its diagnosis For the anatomic position of the ductus arteriosus see Figure 76 page 330

Etiology *Cause* The cause of persistent patency of the ductus arteriosus is not always clear *Frequently it appears to be a compensatory condition in* the presence of some serious cardiovascular defect like infantile coarctation of the aorta or transposition of the great arterial trunks in other cases it is due to an unexplained arrest of development

Age Beginning at birth it may last through a long life It has been noted most often in children and young adults the mean age at death of 92 cases of simple patency in Abbott s series being 24 years It is frequently found in old people the oldest autopsied cases on record being 66 years (Josefson 1897 White 1928) a man with this condition still in good health at 75 years has been followed by the author for 27 years while another case reported by Walker and Ellis in 1941 then in good health at the age of 73 died suddenly

at the age of 78 five years later while mowing his lawn (there was no autopsy —personal communication)

Sex Patency of the ductus arteriosus has been found more often in the female sex in the ratio of 2 to 1 (55 to 29 in Abbott s series of 92 cases of simple patency in which the sex was stated and 333 to 145 in Gross series of 478 cases—Gross personal communication 1951)

Pathology The patency of the ductus arteriosus varies very much in degree, from that of a fine canal barely admitting a small probe or bristle to that of large caliber easily admitting pencil or finger It may be very short so that there is hardly more than a direct opening between contiguous aorta and pul monary artery or it may be several centimeters long usually it is ½ to 2 cm long It may be cylindrical in shape funnel shaped or conical with wider end at the aorta or it may be dilated to form a kind of aneurysm In patency of the ductus arteriosus of long duration or of marked degree especially in the combination of these conditions the pulmonary artery is dilated and both ventricles are enlarged with hypertrophy and dilatation the blood flow from aorta to pulmonary artery increasing the work of both ventricles in such cases the right ventricle has to overcome the pressure directed against its own blood stream and the increased blood flow through the lungs and the left ventricle has to increase its output to make up for the diversion of a considerable amount of blood from the systemic circulation It has been estimated that as much as 25 to 75 per cent of the blood pumped out by the left ventricle may be diverted into the pulmonary circulation via a patent ductus arteriosus Atheroma with calcification is commonly found in the patent ductus arteriosus especially at its mouth in the aorta and often also about its orifice in the pul monary artery *Very rarely spontaneous thrombosis may obliterate the ductus*

The ratio of complicated to uncomplicated patency of the ductus arteriosus is about 2 to 1 In Abbott s series of 150 complicated cases it was found asso ciated with coarctation of the aorta 13 times (6 out of 70 cases of the adult type 7 out of 9 of the infantile type) with complete transposition of the great arterial trunks in 33 cases with pulmonary atresia 28 times with pulmonary stenosis 12 times and with tricuspid atresia 6 times

The ductus arteriosus may take an anomalous course or even be entirely absent Rarely it gives off the left subclavian artery

Symptoms There are no symptoms of patency of the ductus arteriosus itself except in a rare patient who is conscious of the harsh murmur and thrill caused by the rush of blood through the ductus and in occasional cases where the ductus is so large that there is retardation of growth or when dyspnea develops because the heart fails as it would from aortic regurgitation or a large arterio venous communication

Signs Usually pathognomonic evidence of the condition is present There are two important signs one diagnostic the other suggestive when both are present *the diagnosis of patent ductus arteriosus may be regarded as certain*

The first sign is a continuous murmur usually loud with systolic accentu ation maximal over and often limited to the region of the pulmonary artery

at the second rib and intercostal space just to the left of the sternum and not so loud in the neck and generally attended by a palpable thrill (in the absence of evidence of rupture of aorta into pulmonary artery) This murmur has been variously described as resembling the sound of a humming top of a mill wheel or other machinery of a train in a tunnel or of rolling thunder It is almost invariably harsh rarely blowing In cases with a right aortic arch the continuous murmur is heard over the patent ductus at the right of the upper sternum instead of at the left In some cases with wide ductus patency and a dilated left ventricle there may also be heard a mitral middiastolic murmur simulating mitral stenosis

The second important sign is roentgenologic consisting of unusual prominence of the heart shadow in the region of and just above the pulmonary artery (Figure 80) without increase in the size of the left atrium pointing to mitral stenosis and without cyanosis which might result from pulmonary endarteritis obliterans This abnormal bulging of the left upper border of the heart shadow is more pronounced in some cases of patency of the ductus



FIG 80 Roentgenogram of thorax in case of congenital patency of the ductus arteriosus Note the bulge in the region of the pulmonary artery J W male now 75 years with characteristic machinery murmur This film was taken 13 years ago but there has been no change since

arteriosus than in any other condition except that of interatrial septal defect which presents much larger shadows of both pulmonary artery and lung hilus shadows without a continuous murmur *If there is but a narrow lumen through the patent ductus the roentgen ray sign may be minimal or absent while the typical murmur may be marked* If on the other hand there is a very wide lumen with much blood flow the roentgen ray sign is marked and the murmur minimal or absent. In infants and rarely in young children the murmur may *be absent or but slight and only systolic in time during the first few years of life* in adults it is almost invariably present as a typical continuous murmur, but there are rare exceptions with systolic murmur alone

Other signs are those associated with cardiac enlargement which is found in some of the cases various complications and in a few cases a full pulse pressure due to low diastolic pressure when the patency is so wide that there *is considerable aortic regurgitation into the pulmonary artery in* diastole a wide pulse pressure in patency of the ductus arteriosus is however not the rule and a water hammer pulse is very rare

Course, complications, and prognosis *Patency of the ductus arteriosus may* be a condition compensating for the presence of some serious congenital defect like transposition of the great arterial trunks thereby helping together with septal defects to prolong life, in such cases however *life is short at best* lasting only a few years Uncomplicated patency may or may not be an important burden for the heart If it is of large caliber it is a serious condition leading to considerable cardiac enlargement and failure in youth if it is of small caliber it may limit neither activity nor duration of life death in old age being caused by some noncardiac disease The oldest cases proved at autopsy were 66 years of age at death but two other cases have been known to have reached the middle or upper seventies (see above under etiology are) Always however patency of the ductus arteriosus is something of a menace because of the likelihood of invasion by subacute bacterial (Streptococcus viridans) endarteritis which used to end fatally in the course of months just as did subacute bacterial endocarditis with which it may be associated In Abbott s series of 92 primary cases of ductus arteriosus patency death was ascribed to subacute bacterial endarteritis in nearly one quarter while Gelfman and Levine (1942) found 4 such cases (29 per cent) among 14 patients with patency of the ductus

Rupture of a dilated pulmonary artery due to ductus arteriosus patency has been observed as a rare complication Also paradoxical embolism has been noted thrombi from the left atrium or vegetations from the mitral or aortic valves entering the pulmonary circulation by way of the patent ductus *arteriosus A reversal of current may sometimes occur* generally as a terminal event when the blood pressure in the pulmonary circulation for any reason exceeds that in the systemic circuit in infants there may be transient attacks *of dyspnea and cyanosis* when the pulmonary pressure is raised by crying and by holding the breath during nursing Of 92 cases of Abbott s series death in 40 was sudden or due to myocardial failure in 21 to bacterial endarteritis or

endocarditis in 3 to a cerebral lesion in 3 to bronchopneumonia and in the remainder unstated

Treatment A decade ago there was finally introduced what had been prophesied namely specific treatment for patency of the ductus arteriosus Surgical interference to ligate the ductus was successfully accomplished and a new and dramatic era in the treatment of congenital heart disease began (Gross and Hubbard 1939) The operation has now been carried out in many hundreds of cases by various surgeons throughout this country and abroad with very low mortality and with excellent results Transection rather than simple ligation is now recommended by Gross (1947) although excellent results have been obtained by ligation Surgical correction is now definitely indicated in all children and young adults to relieve the heart of strain and to avert the dangerous and common complication of subacute bacterial (Streptococcus viridans) endarteritis but it must be recognized that there are some patients in whom the condition is inoperable (Shapiro and Keys 1943) and that there still exists in any case a definite operative risk Surgery has also been proved (Touroff and Vesell 1940 and 1942 Bourne 1941) to have a place with or without chemotherapy in the cure of subacute bacterial infection of the ductus and pulmonary artery It is striking to note the disappearance of murmur and thrill after ligation of the ductus and in those cases with cardiac enlargement and increased pulse pressure even of such signs too and on occasion even of a mitral middiastolic murmur due to left ventricular dilatation In those cases not operated upon protection against infection and exhaustion is advisable The routine use of penicillin to ward off bacterial endarteritis during infections and surgical procedures including tooth extraction is to be recommended as in the case of a ventricular septal defect (q v)

Differential diagnosis In infants the condition may be undiagnosable In adults the distinctive murmur is almost invariably present this murmur must be differentiated from the venous hum sometimes heard in the neck especially on the right side in children which hum may be transmitted downward over the upper chest but is quickly obliterated by compression of the neck veins and it must also be distinguished from the murmur of an arteriovenous aneurysm uncommon in the upper chest and usually located on the right side A rare condition accompanied by the continuous murmur characteristic of patency of the ductus arteriosus both in position and in character is rupture of an aortic aneurysm into the pulmonary artery the differentiation can be made by analysis of the clinical course The roentgen ray sign of marked prominence of the pulmonary artery though helpful is not pathognomonic of patency of the ductus arteriosus for mitral stenosis pulmonary fibrosis or endarteritis obliterans and interatrial septal defects must be excluded before a sure diagnosis is justifiable

Other Communications Between Aorta and Pulmonary Artery

The other communications between aorta and pulmonary artery are much less common The first is the serious condition of a common arterial trunk (truncus arteriosus communis) with its accompanying intense cyanosis absence of lung hilar shadows, and short life (averaging but 4 years in 21 cases analyzed by Abbott) A second is an opening between these two vessels above the valves usually small and not so important (in Abbott s series 10 cases with survival to 48 years in the oldest) The third is a defect between the right sinus of Valsalva and the right ventricle with or without an associated slight interventricular septal defect just below the valve or between the posterior sinus and the right atrium The defect may exist from birth or there may be in early life simply a thinned wall or aneurysm which may rupture fatally into the right ventricle (Hirschboeck 1942) There are no symptoms caused by these anomalies The signs in cases of the second and *third* categories above in which tnere are definite though small openings are much like those of patency of the ductus arteriosus with loud continuous murmur lower in position and very near the ear The cardiac strain results in enlargement but the particular danger appears to lie in a serious complication of bacterial infection of the walls of the defect

CONGENITAL ANOMALIES OF THE VEINS

Congenital anomalies of the veins are of little or no clinical importance They are frequent in the case of the small veins and rare in the case of the venae cavae and chief pulmonary veins The commonest defect of the great systemic veins is persistence of the left superior vena cava emptying into the right atrium by way of the coronary sinus (36 cases in Abbott s series 27 of which complicated other defects) associated with it in most cases is the usual (right) superior vena cava, but sometimes it is alone and receives blood from the right side by way of an extensively developed vena azygos major In rare cases the single superior vena cava or the inferior vena cava is displaced to the left and opens into both atria at the point of a septal defect Rarely also the left hepatic vein persists and empties into the anomalous left superior vena cava which thus represents the persistent left sinus venosus of the embryo Many different variations are possible in the case of the pulmonary veins (58 cases total in Abbott s series all but 4 complicating other defects) The two right or two left veins sometimes coalesce before entering the left atrium or one or more of the pulmonary veins may empty into the right side of the heart into the persistent left superior vena cava into the normal superior vena cava or into the innominate or hepatic vein *Almost always* there are cardiac anomalies associated with congenital abnormalities of the venae cavae and with the more important abnormalities of the pulmonary veins Symptoms signs course and prognosis depend on these other anomalies and not on the venous defects The diagnosis of uncomplicated congenital defects of the great veins has now become possible in some cases by

means of cardiac catheterization and by detailed x ray studies including angio cardiography

CONGENITAL ANOMALIES OF THE CORONARY VESSELS

Most anomalies of the coronary arteries and veins are of no clinical im portance and are simply postmortem curiosities These include extra coronary mouths (for example the left circumflex coronary artery may arise directly from the aorta) one coronary mouth giving rise to both right and left coronary arteries and unusual course and branching of the vessels Rarely however a serious anomaly occurs this consists most frequently of the origin of the left coronary artery from the pulmonary artery which results in cardiac enlarge ment with hypertrophy and dilatation of the left ventricle myocardial necrosis and fibrosis and early death in the course of the first few months of life One notable case was of a baby boy dying at the age of four months who suffered from attacks during life which closely resembled angina pectoris and showed an electrocardiogram with inverted (coronary) *T* waves in Leads 1 and 2 (Bland White and Garland 1933) Other cases have since been reported one diagnosed antemortem (Eidlow and Mackenzie 1946)

The most common important anomaly of the coronary veins is the per sistence of the left superior vena cava (mentioned above) which takes the place of the coronary sinus this anomaly has however no clinical significance A very rare anomaly is the drainage of the coronary sinus into the left auricle

BIBLIOGRAPHY

CONGENITAL CARDIOVASCULAR DEFECTS

SEE ALSO GENERAL REFERENCES FOLLOWING CHAPTER 2 AND REFERENCES IN CHAPTERS 7 AND 9

General

Abbott M E *Atlas of Congenital Cardiac Disease* American Heart Association New York 1936

Abbott M E and Dawson W T "The Clinical Classification of Congenital Cardiac Disease with Remarks upon Its Pathological Anatomy Diagnosis and Treatment *Internat Clin* 1924 IV 156

Abbott M E and Weiss E "The Diagnosis of Congenital Cardiac Disease *Blumer's Bedside Diagnosis* Philadelphia, 1928

Baillie M *The Morbid Anatomy of Some of the Most Important Parts of the Human Body* J Johnson and G Nicol London 2nd ed 1797 (1st ed 1793) Chapters 1 and 2

Farber S and Hubbard, J "Fetal Endomyocarditis Intra Uterine Infection as Cause of Congenital Cardiac Anomalies" *Am J M Sc* 1933 CLXXXVI 705

Farre J R *Pathological Researches Essay I On Malformations of the Human Heart* Longman Hurst Rees Orme Brown London 1814

Futcher P H and Southworth H "Arachnodactyly and Its Medical Complications *Arch Int Med* 1938 LXI 693

Gelfman R and Levine S A "Incidence of Acute and Subacute Bacterial Endocarditis in Congenital Heart Disease" *Am J M Sc* 1942 CCIV 324

Gintrac E *Observations et Recherches sur la Cyanose ou Maladie Bleue* J Pinard Paris 1824

Gregg N M Congenital Cataract Following German Measles in the Mother *Ophth Soc Australia* 1941 III 35
Harris J S and Farber S Transposition of the Great Cardiac Vessels with S Reference to the Phylogenetic Theory of Spitzer *Arch Path* 1939 XXVIII
Keith A The Hunterian Lectures on Malformations of the Heart *Lancet* 19C 359 433 and 519
Laubry C and Pezzi C *Traite des Maladies Congenitales du Coeur* J B Bailli Fils Paris 1921
Levinson S A Congenital Heart Disease as Cause of Sudden Unexpected Dea Children Under One Year of Age *Am J Clin Path* 1941 XI 741
McLean S A Cardiac Development Defect with Return to Normal *J A M A* LXXIV 1229
Marfan A B Un cas de deformation congenitale des quatre membres plus pron aux extrémités caracterisee par l allongement des os avec un certain degre d amin ment" *Bull et mem soc med hop d Paris* 1896 XIII 220
Peacock T B *On Malformations of the Human Heart etc with Original Case Illustrations* John Churchill and Sons London 2nd ed 1866 (1st ed 1858)
Rosler H "Beitrage zur Lehre von den angeborenen Herzfehlern I Uber die Ron befunde bei angeborenen Herz Gefässmissbildungen (Herzfehlern) *Wien Ar inn Med* 1928 XV 487
Spitzer A Uber den Bauplan des normalen und missbildeten Herzens (Versuch phylogenetischen Theorie) *Virch Arch f path Anat* 1923 CCXLIII 81
Swan C Tostevin A L Moore B Mayo H and Barham Black G H Cong Defects in Infants Following Infectious Diseases During Pregnancy With Sp Reference to the Relationship between German Measles and Cataract Deaf Mu Heart Disease and Microcephaly and to the Period of Pregnancy in Which the O rence of Rubella Is Followed by Congenital Abnormalities" *M J Australia* II 201
White P D and Jones T D "Heart Disease and Disorders in New England" *Heart J* 1928 III 302

Recent References (1944–1950)

Alexander F and White P D Four Important Congenital Cardiac Conditions C ing Cyanosis to be Differentiated from the Tetralogy of Fallot Tricuspid Atr Eisenmenger s Complex Transposition of the Great Vessels and a Single Ventri *Ann Int Med* 1947 XXVII 64
Barclay A E Franklin K J and Prichard M M L *The Foetal Circulation Cardiovascular System and the Changes That They Undergo at Birth* Black Scientific Publications Ltd Oxford 1944
Campbell M "Genetic and Environmental Factors in Congenital Heart Di e *Quart J Med* 1949 XVIII 379
Clawson B J "Types of Congenital Heart Disease in 15 597 Autopsies *J La* 1944 LXIV 134
Dexter L Cardiac Catheterization in Diagnosis of Congenital Heart Disease" *New York Acad Med* 1950 XXVI 93
Dexter L Haynes F W Burwell C S Eppinger E C Seibel R E and Ev J M Studies of Congenital Heart Disease I Technique of Venous Catheteriza as a Diagnostic Procedure" *J Clin Investigation* 1947 XXVI 547
III Venous Catheterization as a Diagnostic Aid in Patent Ductus Arterio Tetralogy of Fallot Ventricular Septal Defect and Auricular Septal Defect" *Il* 1947 XXVI 561
Donzelot E Emam Zade A M Heim de Balsac R and others L angiocardiogra dans les cardiopathies congenitales interpretation valeur indications" *Semaine Hop de Paris* 1949 XXV 2309
Dry T J et al *Congenital Anomalies of the Heart and Great Vessels* Charle Thomas Publisher Springfield Illinois 1948
Gates E M Rogers H M and Edwards J E "Syndrome of Cerebral Abscess Congenital Cardiac Disease" *Proc Staff Meet Mayo Clin* 1947 XXII 401

Gregg N M "Rubella During Pregnancy of the Mother with Its Sequelæ of Congenital Defects in the Child *M J Australia* 1945 I 313

McQuiston W O "Anesthesia in Cardiac Surgery Observations on Three Hundred and Sixty two Cases *Arch Surg* 1950 LXI 892

Mannheimer E *Morbus Caeruleus An Analysis of 114 Cases of Congenital Heart Disease with Cyanosis* S Karger Basle Suisse and New York 1949

Maronde R F Brain Abscess and Congenital Heart Disease *Ann Int Med* 1950 XXXIII 602

Mlezoch F and Salzmann F "Thorakoskopie bei angeborenen Herzfehlern *Wien Ztschr fur inn Med* 1950 XXXI 442

Murray G "Closure of Defects in Cardiac Septa *Ann Surg* 1948 CXXVIII 843

Paul O Myers G S and Campbell J A 'The Electrocardiogram in Congenital Heart Disease A Preliminary Report *Circulation* 1951 III 564

Perez de los Reyes R de la Torre H and Douglas R Remarks About 500 Cases of Cardiovascular Congenital Malformations Examined in the Cardiological Department of the Infants Municipal Hospital in Habana During the Last Thirteen Years" *Am Heart J* 1949 XXXVII 661

Taussig, H B *Congenital Malformations of the Heart* The Commonwealth Fund New York, 1947

Analysis of Malformations of the Heart Amenable to a Blalock Taussig Operation" *Am Heart J* 1948 XXXVI 321

Thordarson O "Clinical Studies on Relative Incidence of Congenital Heart Disease *Acta med Scandinav* 1947 CXXVII 233

Tobin J R Jr Bay E B and Humphreys E M Marfan s Syndrome in Adult Dissecting Aneurysm of Aorta Associated with Arachnodactyly" *Arch Int Med* 1947 LXXX 475

Tubbs O S "The Surgery of Congenital Heart Disease *Brit Heart J* 1948 X, 77

Wesselhoeft C. Rubella (German Measles) and Congenital Deformities *New England J Med* 1949 CCXL 258

Dextrocardia

Churchill E D and Adams F D "Situs Inversus Sinusitis Bronchiectasis Report of 5 Cases Including Frequency Statistics" *J Thoracic Surg* 1937 VII 206

Rosler H Beitrage zur Lehre von der angeborenen Herzfehlern VI Uber die angeborene isolierte Rechtslage des Herzens *Wien Arch f inn Med* 1930 XIX 505

Congenital Hypertrophy (Including the So-called Idiopathic)

(See also under Coronary Anomalies)

Howland J Idiopathic Hypertrophy of the Heart in Young Children *Contributions to Medical and Biological Research* dedicated to Sir William Osler 1919 I 582

Hubbard J P Paroxysmal Tachycardia and Its Treatment in Young Infants" *Am J Dis Child* 1941 LXI 687

Kugel M A and Stoloff E G "Dilatation and Hypertrophy of the Heart in Infants and in Young Children With Myocardial Degeneration and Fibrosis (So-Called Congenital Idiopathic Hypertrophy) *Am J Dis Child* 1933 XLV 828

Pompe J C Hypertrophie idiopathique du coeur" *Ann d'anat path et d'anat norm med chir* 1933 X 23

von Gierke F Hepato-nephromegalia glycogenica *Beitr path Anat u z allg Path* 1929 LXXXII 497

Interatrial Septal Defects

Abbott M E Two Cases of Widely Patent Foramen Ovale" *Bull Internat A M Museums* 1915 V 129

Askey J M and Kahler J E "Longevity in Extensive Organic Heart Lesions A Case of Lutembacher s Syndrome in a Man Aged 72 *Ann Int Med* 1950 XXXIII 1031

Barber J M Magidson O and Wood P Atrial Septal Defect With Special Reference to the Electrocardiogram the Pulmonary Artery Pressure and the Second Heart Sound" *Brit Heart J* 1950 XII 277

Bedford D E Papp C and Parkinson J Atrial Septal Defect *Brit Heart J* 1941 III 37
Bonnabel J *Contribution à l etude de quelques affections congénitales du coeur compatibles avec l existence et de leur pronostic* Thesis Paris 1906–7
Christie A Normal Closing Time of the Foramen Ovale and the Ductus Arteriosus An Anatomic and Statistical Study" *Am J Dis Child* 1930 XL 323
Cournand A Motley H L Himmelstein A Dresdale D and Baldwin J Recording of Blood Pressure from the Left Auricle and the Pulmonary Veins in Human Subjects with Interauricular Septal Defect *Am J Physiol* 1947 CL 267
Dow J W and Dexter L Circulatory Dynamics in Atrial Septal Defect *J Clin Investigation* 1950 XXIX 809
Ellis F R Greaves M and Hecht H H Congenital Heart Disease in Old Age Interauricular Septal Defect with Mitral and Tricuspid Valvulitis *Am Heart J* 1950 XL 154
Firket C Examen anatomique d un cas de persistance du trou ovale de Botal avec lesions valvulaires considerables du coeur gauche chez une femme de 74 ans *Ann soc med-chir* Liege 1880 XIX 188
Ingham D W Paradoxical Embolism *Am J M Sc* 1938 CXCVI 201
Lut mbacher D De la stenose mitrale avec communication interauriculaire" *Arch d mal d coeur* 1916 IX 237
McGinn S and White P D Interauricular Septal Defect Associated with Mitral Stenosis *Am Heart J* 1933 IX 1
Patten B M "Closure of Foramen Ovale *Am J Arat* 1931 XLVIII 19
Roesler H "Interatrial Septal Defect *Arch Int Med* 1923 LIV 339
Seib G A Incidence of Patent Foramen Ovale Cordis in Adult American Whites and American Negroes" *Am J Anat* 1934 LV 511
Selzer A and Lewis A E "The Occurrence of Chronic Cyanosis in Cases of Atrial Septal Defect *Am J M Sc* 1949 CCXVIII 516
Swan H Maresh G Johnson M E and Warner G "The Experimental Creation and Closure of Auricular Septal Defects" *J Thoracic Surg* 1950 XX 542
Uhley M H "Lutembacher s Syndrome and a New Concept of the Dynamics of Interatrial Septal Defects" *Am Heart J* 1942 XXIV 315

Interventricular Septal Defects

Donzelot E Emam Zade A M Heim de Balsac R and Kolosy M Le complexe d Eisenmenger Étude de 29 cas *Arch d mal d coeur* 1949 XLII 118
Eisenmenger V Die angeborenen Defecte der Kammerscheidewand des Herzens *Ztschr f klin Med* 1897 XXXII Supplement H ft, 1
Roger H Recherches cliniques sur la communication congénitale des deux coeurs p r inocclusion du septum interventriculaire *Bull d l Acad d med d Paris* 1879 VIII 1074
Rokitansky C *Die Defecte der Scheidewande des Her ens* Braumuller Vienna 1875
Rosedale R S Interventricular Septal Defect Dextroposition of Aorta and Dilatation of Pulmonary Artery Report of Case with Structural Pathogenesis" *Am J Path* 1935 XI 333
Selzer A "Defect of the Ventricular Septum Summary of Twelve Cases and Review of the Literature" *Arch Int Med* 1949 LXXXIV 798
Selzer A and Laqueur G L "The Eisenmenger Complex and Its Relation to the Uncomplicated Defect of the Ventricular Septum Review of Thirty five Autopsied Cases of Eisenmenger s Complex Including Two New Cases" *Arch Int Med* 1951 LXXXVII 218

Pulmonary Stenosis

Blalock A and Kieffer R F Jr "Valvulotomy for Relief of Congenital Valvular Pulmonic Stenosis with Intact Ventricular Septum Report of 19 Operations by the Brock Method" *Ann Surg* 1950 CXXXII 496
Brock R C "Pulmonary Valvulotomy for Relief of Congenital Pulmonary Stenosis" and Surgery of Pulmonary Stenosis" *Brit M J* 1948 I 1121 and 1949 II 399

Brock R C and Campbell M Valvulotomy for Pulmonary Valvular Stenosis *Brit Heart J* 1950 XII 377
Infundibular Resection or Dilatation for Infundibular Stenosis *Ibid* 1950 XII 403
Currens J H Kinney T D and White P D Pulmonary Stenosis with Intact Interventricular Septum Report of Eleven Cases *Am Heart J* 1945 XXX 491
Engle M A and Taussig H B Valvular Pulmonic Stenosis with Intact Ventricular Septum and Patent Foramen Ovale Report of Illustrative Cases and Analysis of Clinical Syndrome *Circulation* 1950 II 481
Genovese P D and Rosenbaum D Pulmonary Stenosis with Survival to the Age of 78 Years" *Am Heart J* 1951 XLI 755
Joly Fr Carlotti J Sicot J R and Piton A Cardiopathies congenitales II Les trilogies de Fallot *Arch d mal d coeur* 1950 XLIII 687
Potts W J Surgical Treatment of Congenital Pulmonary Stenosis *Ann Surg* 1949 CXXX, 342
Potts W J and Gibson S Aortic Pulmonary Anastomosis in Congenital Pulmonary Stenosis Report of Forty five Cases *J A M A* 1948 CXXXVII 343
Potts W J Gibson S Riker W L and Leininger C R Congenital Pulmonary Stenosis with Intact Ventricular Septum *J A M A* 1950 CXLIV 8
Potts W J Smith S and Gibson S Anastomosis of Aorta to Pulmonary Artery" *J A M A* 1946 CXXXII 627
Selzer A Carnes W H Noble C A Jr and others "Syndrome of Pulmonary Stenosis with Patent Foramen Ovale *Am J Med* 1949 VI 3
White P D Hurst J W and Fennell R H Survival to the Age of Seventy five Years with Congenital Pulmonary Stenosis and Patent Foramen Ovale *Circulation* 1950 II 558

Tetralogy of Fallot

Blalock A and Taussig H B Surgical Treatment of Malformations of Heart *J A M A* 1945 CXXVIII 189
Donzelot, E Heim de Balsac R Emam Zade A M Escalle J E and Metianu C Étude de 200 cas de tetrade de Fallot *Arch d mal d coeur* 1949 XLII 98
Fallot A Contribution à l Anatomie pathologique de la Maladie bleue (Cyanose cardiaque) *Marseilles méd* 1888 XXV 77 138 207 270 and 403
Hunter W Three Cases of Malconformation in the Heart *Med obs soc phys London* 1784 VI 291
Sandifort E *Observationes anatomico pathologicae* Ludg Bat P v d Eyk et D Vygh 1777 Chap 1 Fig 1
Stensen Niels (Nicholaus Steno) In Bartholin Thomas *Acta medica et philosophica Hafniencia* 1671-1672 I 202 Reprinted in Stenonis Nicolai *Opera philosophica* 2 49-53 edited by Vilhelm Maar Copenhagen 1910
Talbott J H et al A Record Case of the Tetralogy of Fallot with Comments on Metabolic and Pathologic Studies *Am Heart J* 1941 XXII 754
White P D and Sprague H B The Tetralogy of Fallot Report of a Case in a Noted Musician Who Lived to His Sixtieth Year *J A M A* 1929 XCII 787

Other Valvular and Ostial Defects

Abbott M E On the Relative Incidence and Clinical Significance of a Congenitally Bicuspid Aortic Valve *Libman Anniversary Volumes* 1932 I 1
Campbell J M Artificial Aortic Valve Preliminary Report *J Thoracic Surg* 1950 XIX 312
Donnally H H Congenital Mitral Stenosis Report of a Case of Developmental Mitral Stenosis Combined with Hypoplasia of Left Ventricle and Left Auricle Rudimentary Aorta and Other Developmental Defects" *J A M A* 1924 LXXXII 1318
Ebstein W Ueber einen sehr seltenen Fall von Insuffizienz der Valvula tricuspidalis bedingt durch eine angeborene hochgradige Missbildung derselben *Arch f Anat u Physiol* 1866 p 238
Engle M A Payne T P B Bruins C and Taussig H B Ebstein s Anomaly of the Tricuspid Valve Report of Three Cases and Analysis of Clinical Syndrome" *Circulation* 1950 I 1246

Fell E H Gasul B M Davis C B Jr and Casas R Surgical Treatment of Tricuspid Atresia *Arch Surg* 1949 LIX 445
Gasul B M Fell E H Marino J J and Davis C B Jr Tricuspid Atresia Report of Two Cases of Young Infants with Successful Operation" *Am J Dis Child* 1949 LXXVIII 16
Lewis T and Grant R T Observations Relating to Subacute Infective Endocarditis Part 1 Notes on the Normal Structure of the Aortic Valve Part 2 Bicuspid Aortic Valves of Congenital Origin *Heart* 1923 X 21
Sommers S C and Johnson J M Congenital Tricuspid Atresia *Am Heart J* 1951 XLI 130
Sternberg C "Ueber infravalvulare Konusstenosen Zur Pathologie der Grenze zwischen Herzmuskulatur und Herzskelett (A discussion of subaortic and subpulmonary infundibular stenosis) *Verhandl d deutsch path Gesellsch* 1930 XXV 238
Taussig H B Clinical and Pathological Findings in Congenital Malformations of Heart Due to Defective Development of Right Ventricle Associated with Tricuspid Atresia or Hypoplasia *Bull Johns Hopkins Hosp* 1936 LIX 435
Yater W M and Shapiro M J "Congenital Displacement of the Tricuspid Valve (Ebstein s Disease) Review and Report of a Case with Electrocardiographic Abnormalities and Detailed Histologic Study of the Conduction System *Ann Int Med* 1937 XI 1043

Heart Block

Campbell M Congenital Complete Heart Block *Brit Heart J* 1943 V 15
Carter E P and Howland J A Note Upon the Occurrence of Congenital Atrioventricular Dissociation Report of a Case of Congenital Complete Heart Block *Bull Johns Hopkins Hosp* 1920 XXXI 351
Plant R K and Steven R A Complete A V Block in a Fetus *Am Heart J* 1945 XXX 615
Wilson J G and Grant R T A Case of Congenital Malformation of the Heart in an Infant Associated with Partial Heart Block *Heart* 1926 XII 295 (The first autopsy report)
Yater W M Congenital Heart Block Report of a Case with Incomplete Heterotaxy *Proc Staff Meet Mayo Clin* 1928 III 320

Coarctation of the Aorta

Abbott M E "Coarctation of the Aorta of the Adult Type II Statistical and Historical Retrospect of 200 Recorded Cases with Autopsy of Stenosis or Obliteration of the Descending Arch *Am Heart J* 1928 III 574
Blackford L M Coarctation of the Aorta *Arch Int Med* 1928 XLI 70
Christensen N A and Hines E A Jr Clinical Features in Coarctation of the Aorta A Review of 96 Cases *Proc Staff Meet Mayo Clin* 1948 XXIII 339
Crafoord C and Nylin G "Congenital Coarctation of Aorta and Its Surgical Treatment" *J Thoracic Surg* 1945 XIV 347
Freeman N E Miller E R Stephens H B and Olney M B Retrograde Arteriography in the Diagnosis of Cardiovascular Lesions II Coarctation of the Aorta *Ann Int Med* 1950 XXXII 827
Graybiel A Allen A W and White P D "Histologic Study of Arterioles of Muscle and Skin from Arm and Leg in Individuals with Coarctation of the Aorta" *J Clin Investigation* 1935 XIV 52
Gross R E Surgical Correction for Coarctation of Aorta *Surgery* 1945 XVIII 673
"Coarctation of the Aorta Treatment of One Hundred Cases" *Circulation* 1950 I 41
Johnson J and Kirby C K "Surgical Treatment of Infantile Type of Coarctation of Aorta" *Ann Surg* 1948 CXXVII 1119
Lewis T "Material Relating to Coarctation of the Aorta of the Adult Type" *Heart* 1933 XVI 205
Morgagni J B *De Sedibus et Causis Morborum* Typographia Remondiniani Venice 1761

Nickerson J L Humphreys G H Deterling R A Fleming T C and Mathers J A L "Diagnosis of Coarctation of the Aorta with the Aid of the Low Frequency Critically Damped Ballistocardiograph" *Circulation* 1950 I 1032
Pereiras R and Castellanos A "Retrograde Aortography Its Value in Diagnosis of Coarctation of Aorta by Means of New Indirect Sign *Radiology* 1949 LIII 859
Potts W J "Technic of Resection of Coarctation of Aorta with Aid of New Instruments" *Ann Surg* 1950 CXXXI 466
Reifenstein G H Levine S A and Gross R E Coarctation of the Aorta" *Am Heart J* 1947 XXXIII 146
Steele J M and Cohn A E The Nature of Hypertension in Coarctation of the Aorta *J Clin Investigation* 1938 XVII 514
Taylor B E et al Patent Ductus Arteriosus Associated with Coarctation of the Aorta Report of 2 Cases Studied Before and After Surgical Treatment *Proc Staff Meet Mayo Clin* 1950 XXV 62
Walker W B "Coarctation of the Aorta in Father and Son *New England J Med* 1934 CCXI 1192

Other Anomalies of the Aorta

Arkin A Double Aortic Arch with Total Persistence of the Right and Isthmus Stenosis of the Left Arch A New Clinical and X ray Picture Report of Six Cases in Adults" *Am Heart J* 1936 XI 444
Baer R W Taussig H B and Oppenheimer E H Congenital Aneurysmal Dilatation of Aorta Associated with Arachnodactyly *Bull Johns Hopkins Hosp* 1943 LXXII 309
Bain C W C and Parkinson J "Common Aorto Pulmonary Trunk A Rare Congenital Defect" *Brit Heart J* 1943 V 97
Downing D F Congenital Aortic Septal Defect *Am Heart J* 1950 XL 285
Gross R E and Ware P F Surgical Significance of Aortic Arch Anomalies" *Surg Gynec & Obst* 1946 LXXXIII 435
Herbut P A "Anomalies of Aortic Arch *Arch Path* 1943 XXXV 717
Ingalls N W "Truncus Arteriosus Communis Persistens *Anat Rec* 1915 X 9
King, F H et al "Aortic Septal Defect Simulating Patent Ductus Arteriosus *J Mt Sinai Hosp* 1951 XVII 310
MacGilpin H H Jr 'Truncus Arteriosus Communis Persistens *Am Heart J* 1950 XXXIX, 615
Monie I W and DePape A D J Congenital Aortic Atresia Report of One Case with an Analysis of 26 Similar Reported Cases" *Am Heart J* 1950 XL 595
Morrison R W and Edwards J E "Subaortic Stenosis Report of Two Cases One Associated with Patent Ductus Arteriosus the Other Complicated by Bacterial Endocarditis" *Bull Internat A M Museums* 1950 XXXI 73
Perelman H and Putschar W G J Congenital Communication Between Aorta and Pulmonary Artery Report of a Case and Review of the Literature *Bull Internat A M Museums* 1949 XXX, 1
Rokitansky C *Die Defecte der Scheidewände des Herzens* Braumuller Vienna 1875
Spencer H and Dworken H J Congenital Aortic Septal Defect with Communication Between Aorta and Pulmonary Artery Case Report and Review of Literature *Circulation* 1950 II 880
Sprague H B Ernlund C H and Albright F "Clinical Aspects of Persistent Right Aortic Root" *New England J Med* 1933 CCIX, 679
Wolman, I J Syndrome of Constricting Double Aortic Arch in Infancy *J Pediat* 1939 XIV 527

Transposition of the Great Arterial Trunks

Blalock A and Hanlon C R "Surgical Treatment of Complete Transposition of Aorta and Pulmonary Artery *Surg Gynec & Obst* 1950 XC 1
Harris J S and Farber S "Transposition of Great Cardiac Vessels with Special Reference to Phylogenetic Theory of Spitzer" *Arch Path* 1939 XXVIII 427
Spitzer A "Über den Bauplan des normalen und missbildeten Herzens" *Virch Arch f Path Anat* 1923 CCXLIII 81

Taussig H B Complete Transposition of the Great Vessels *Am Heart J* 1938 XVI 728
Taussig H B and Bing R J Complete Transposition of the Aorta and a Levoposition of the Pulmonary Artery Clinical Physiological and Pathological Findings *Am Heart J* 1949 XXXVII 551

Patent Ductus Arteriosus

Adams F H LaBree J and Stauffer H M Right Heart Catheterization of Aorta Through a Patent Ductus Arteriosus Report of 2 Cases *Pediatrics* 1950 V 390
Botallo Quoted by Puschmann *Handbuch geschichte der medi in* 1903 II 235 footnote 9 (Botallo in his anatomical observations named *L Opera omnia* Vena arteriarum nutrix a nullo Danielis and Abrahmi Gaasbeeck 1660 p 66)
Bourne G et al Ligation and Chemotherapy for Infection of Patent Ductus Arteriosus *Lancet* 1941 II 444
Burwell C S Eppinger E C and Gross R E 'The Effects of Patency of the Ductus Arteriosus on the Circulation *J Clin Investigation* 1940 XIX 774 and 1941 XX 127
Donovan M S Neuhauser E D and Sosman M C Roentgen Signs of Patent Ductus Arteriosus Summary of 50 Surgically Verified Cases " *Am J Roentgenol* 1943 L 293
Fishman L and Silverthorne M C "Persistent Patent Ductus Arteriosus in the Aged Including the Report of the Oldest Case on Record with Diagnosis Confirmed Post Mortem *Am Heart J* 1951 XLI 762
Graybiel A Strieder J W and Boyer N H An Attempt to Obliterate the Patent Ductus Arteriosus in a Patient with Subacute Bacterial Endocarditis *Am Heart J* 1938 XV 621
Gross R E Complete Division for Patent Ductus Arteriosus *J Thoracic Surg* 1947 XVI 314
Gross R E and Hubbard J P "Surgical Ligation of a Patent Ductus Arteriosus Report of First Successful Case *J A M A* 1939 CXII 729
Josefson A Offenstehender Ductus Botalli nebst Atherom in den Asten der Arteria pulmonalis " *Nord med ark* Stockholm 1897 n s VII No 10 p 1
Kjaergaard H "Patent Ductus Botalli in Three Sisters *Acta med Scandinav* 1946 CXXV 339
Myers G S et al Atypical Patent Ductus Arteriosus with Absence of the Usual Aortic Pulmonary Pressure Gradient and of the Characteristic Murmur " *Am Heart J* 1951 XLI 819
Pritchard W H Brofman B L and Hellerstein H K Clinical Studies in Reversal of Flow in Patent Ductus Arteriosus " *J Lab & Clin Med* 1950 XXXVI 974
Ravin A and Darley W Apical Diastolic Murmurs in Patent Ductus Arteriosus *Ann Int Med* 1950 XXXIII 903
Shapiro M J and Keys A "Prognosis of Untreated Patent Ductus Arteriosus and Results of Surgical Intervention Clinical Series of 50 Cases and Analysis of 139 Operations *Am J M Sc* 1943 CCVI 174
Touroff A W S and Vesell H "Experiences in Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Compli ating Patent Ductus Arteriosus *J Thoracic Surg* 1940 X 59
Walker G C and Ellis L B "The Familial Occurrence of Congenital Cardiac Anomalies " *Proc New England Heart A* 1940–41 p 26
White P D "Patent Ductus Arteriosus in a Woman in Her Sixty sixth Year " *J A M A* 1928 XCI 1107

Defects of the Great Veins

Abbott O A "Congenital Aneurysm of Superior Vena Cava Report of One Case with Operative Correction " *Ann Surg* 1950 CXXXI 259
Curtis A C and Helms R W Congenital Absence of the Valves in the Veins as a Cause of Varicosities " *Arch Dermat & Syph* 1947 LV 639
Dotter C T Hardisty N M and Steinberg I "Anomalous Right Pulmonary Vein Entering the Inferior Vena Cava Two Cases Diagnosed During Life by Angiocardiography and Cardiac Catheterization " *Am J M Sc* 1949 CCXVIII 31

Gi espie J E O'N Pulmonary Venous Return via Superior Vena Cava *Brit Heart J* 1941 III 241
MacCready P B Anomalies of the Pulmonary Veins *Bull Johns Hopkins Hosp* 1918 XXIX 271
Papez J W "Two Cases of Persistent Left Superior Vena Cava in Man *Anat Rec* 1938 LXX 191
Smith J C Anomalous Pulmonary Veins *Am Heart J* 1951 XLI 561
Young M O Common Trunk of Pulmonary Veins Tributary to Portal Vein, with Multiple Cardiac Anomaly *Arch Path* 1947 XLIV 169

Coronary Anomalies

Bland E F White P D and Garland J Congenital Anomalies of the Coronary Arteries Report of an Unusual Case Associated with Cardiac Hypertrophy *Am Heart J* 1933 VIII 787
Eidlow S and Mackenzie E R Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery Report of a Case Diagnosed Clinically and Confirmed by Necropsy *Am Heart J* 1946 XXXII 243
Gasul B M and Loeffler E "Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery (Bland White Garland Syndrome) Report of Four Cases *Pediatrics* 1949 III 498
Jordan R A Dry T J and Edwards J E "Cardiac Clinics CXXXVI Anomalous Origin of the Right Coronary Artery from the Pulmonary Trunk *Proc Staff Meet Mayo Clinic* 1950 XXV 673
Krumbhaar E B and Ehrich W E Varieties of Single Coronary Artery in Man Occurring as Isolated Cardiac Anomalies *Am J M Sc* 1938 CXCVI 407
Smith J C Review of Single Coronary Artery with Report of 2 Cases *Circulation* 1950 I 1168
White N K and Edwards J E "Anomalies of the Coronary Arteries Report of Four Cases" *Arch Path* 1948 XLV 766

Miscellaneous

Chiari H Ueber Netzbildungen im rechten Vorhofe des Herzens *Beitr z path Anat u allg Path* 1897 XXII 1
Collins D C Anomalous Papillary Muscle Attached to Pulmonary Valve of Heart *Am Heart J* 1931 VII 79
Gross R E Bill A H Jr and Peirce E C Methods for Preservation and Transplantation of Arterial Grafts Observations on Arterial Grafts in Dogs Report of Transplantation of Preserved Arterial Grafts in Nine Human Cases *Surg Gynec & Obst* 1949 LXXXVIII 689
Gross R E and Neuhauser E B D Compression of Trachea or Esophagus by Vascular Anomalies Surgical Therapy in 40 Cases *Pediatrics* 1951 VII 69
Hamilton W F and Byers R Aortic Disease with Anomalous Signs Due to Aberrant Chordae Tendineae *Montreal M J* 1899 XXVIII 508
Hirschboeck F J Aneurysm of One of the Sinuses of Valsalva Caused by a Congenital Lesion Case Report *Am Heart J* 1942 XXIV 550
Huchard H Contribution a l etude clinique des tendons aberrants du coeur *Rev de med* 1893 XIII, 113
Lindeboom G A and Bouwer W F Dissecting Aneurysm (and Renal Cortical Necrosis) Associated with Arachnodactyly (Marfan s Disease) *Cardiologia* 1949 XV 12
Parsons C G Cor Triatriatum Concerning the Nature of an Anomalous Septum in the Left Auricle *Brit Heart J* 1950 XII 327
Rogers H M and Edwards J E "Cor Triloculare Biatriatum An Analysis of the Clinical and Pathologic Features of Nine Cases *Am Heart J* 1951 XLI 299
Sinclair J G "A Five-Chambered Human Heart" *Anat Record* 1944 XC, 41
Soulie P Servelle M Barreau A Schweisguth O and Rougeulle J "Greffes arterielles dans le traitement des malformations congenitales du coeur" *Presse med* 1950 LVIII 761
Yater W M "Variations and Anomalies of the Venous Valves of the Right Atrium of the Human Heart *Arch Path* 1929 VII 418

CHAPTER 14

RHEUMATIC HEART DISEASE

Introduction Although at present apparently and happily on the decline one of the three most common and serious types of heart disease is rheumatic, the other two are hypertensive and coronary The relative incidence of these types varies greatly in different parts of the world in fact in different parts of the United States of America for example in New England more than twenty years ago the proportions were recorded as approximately 40, 29 and 36 per cent respectively with some overlapping of the latter two (White and Jones 1928) in Virginia 22, 46 and 46 per cent respectively (Wood Jones and Kimbrough 1926) in San Francisco somewhat more recently 22, 22 and 40 per cent respectively (Geiger et al 1936), and in Texas 10, 45 and 24 per cent for the whites and 4, 51 and 6 per cent for the Negroes (Stone and Vanzant 1927) A reappraisal of these percentages is now in order because of the possibility of a changing incidence as well as of more accurate statistics Recent papers for example report 13 8 per cent among 436 cases of organic heart disease for Southwestern Virginia (Glendy 1948) 117 cases of rheumatic heart disease (11 per cent) as found among 1 045 cardiac autopsies in another southern group (Holoubeck and Holoubeck 1947) and 26 9 per cent of 519 cardiacs in the Rocky Mountains (Cannon 1946) A recent review of 3 000 cases of heart disease in New England (White 1951) has given percentages of 23 5, 26 2 and 48 5 respectively for rheumatic hypertensive and coronary heart disease Thus climatic conditions and to a much less extent race have seemed to be important controlling factors as will be noted in more detail later Other relationships that have become more and more evident in the past few decades are familial susceptibility social and economic status with particular reference to crowding and the hemolytic streptococcus as an exciting factor these will be discussed shortly

One of the most important reasons why rheumatic heart disease is so serious is the fact that it is particularly a disease of youth crippling and killing many children and young adults As a result many medical investigators and special

practitioners and social workers have undertaken campaigns to study the various problems involved and to reduce this menace and scourge which has assumed somewhat the role once held by the white plague tuberculosis During the fifteen year age period from 5 to 20 rheumatic fever with heart disease is in the United States the leading cause of death and at ages 20 to 25 it is second only to tuberculosis (Armstrong and Wheatley *Studies in Rheumatic Fever* Metropolitan Life Insurance Company Nov 1944) In New York City in 1938 there were 1 105 deaths reported from rheumatic fever and rheumatic heart disease as compared with a combined total of 247 from whooping cough meningitis measles diphtheria scarlet fever and poliomyelitis (see Figure 81)

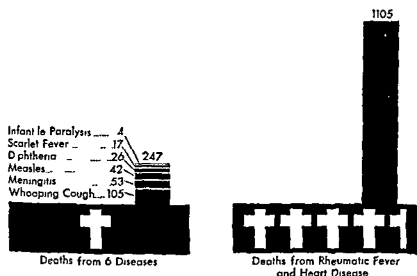


FIG 81 Deaths from rheumatic fever and heart disease compared with deaths from six other common infectious diseases New York City 1938 Data compiled by Dr Homer Swift (Kindness of Dr David I Rutstein and the American Public Health Association New York)

Already however either as the result of special efforts or because of an amelioration of the rheumatic infection itself or both or most likely of all because of considerable improvement in living conditions there is some indication that in the last three decades (1920 to 1950) there has been a slight but definite decline both in the severity and in the incidence of rheumatic heart disease (Hedley 1939 Wheatley 1949) evidences of which have been a drop from 27 cases per thousand patients in the wards of the Massachusetts General Hospital during the years from 1927 to 1930 to 22 cases per thousand during the years from 1937 to 1940 and finally 15 cases per thousand during the years from 1947 to 1950 a decrease from 26 cases per thousand at the Boston Floating Hospital in the years 1933 to 1937 to 9 per thousand from 1943 to 1947 and to 6 per thousand in 1948 and 1949 (kindness of Dr

James Baty) the complete clearing of a formerly long waiting list of children with rheumatic fever for admission to the House of the Good Samaritan in Boston, the decrease in rheumatic heart disease found recently in the school children of Denver Colorado and a drop of relative incidence of rheumatic heart disease among cardiac admissions to the John Sealy Hospital in Galveston from 7 6 per cent in the decade 1920–1929 to 2 1 per cent in the decade 1930–1939 (Decherd and Herrmann, 1943)

The broad term rheumatic heart disease includes acute subacute and chronic involvement of the heart of the 'rheumatic type (as discussed under the heading Pathology to follow) whether or not a clear cut history of rheumatic fever can be elicited The rheumatic infection itself is manifested by a widespread reaction of the tissues throughout the body in this respect resembling tuberculosis and syphilis on the one hand and allergy on the other In fact the terms rheumatic granulomatosis the rheumatic state and rheumaticosis have been suggested as better than the usual expressions rheumatic polyarthritis rheumatic fever, and the rheumatic infection (Fahr 1929 Coburn 1931 Graham 1932)

Etiology *Cause* The cause of the rheumatic infection that plays such havoc in the heart is not yet clear It is the subject of intensive research at the present time and the solution of the problem is awaited with the keenest interest. Streptococci of various types have been considered in some way responsible for many years and especially the hemolytic streptococcus (Coburn and others) the general consensus of opinion is that the Streptococcus hemolyticus is the chief exciting factor which precipitates the so-called rheumatic state throughout the body particularly in the heart Other exciting factors have however been noted such as typhoid vaccine (Bland and Jones 1935) and even injuries suggesting that the exciting factor is not specific nevertheless an acute streptococcus infection appears responsible in the vast majority of the cases The finding of streptococci or other bacteria in the blood joint fluid or pericardial or pleural fluid of acute rheumatic cases has been occasionally reported but is not considered of primary importance any more than the finding of immunologic reactions in tissues or blood A decade or two ago a virus origin of the disease was suggested but this has never been confirmed Whether the tissue reactions throughout the body are due directly to bacterial toxin or result indirectly from an intermediary agent or as an allergic response has not yet been settled Something akin to the last mentioned hypothesis with particular involvement of the body s collagen is at present thought to be most likely but much research on this problem is in progress

In recent years there have arisen interesting speculations concerning the possible role in the production of rheumatic fever of the action of hyaluronidase an enzyme on hyaluronic acid a mucopolysaccharide which with chondroitin sulfate is an important element in the ground substance of connective tissue synovial fluid and certain other parts of the body Certain strains of hemolytic streptococci produce hyaluronic acid and hyaluronidase and

salicylates have been reported to exert an antihyaluronidase effect The possible etiologic relationships suggested by these findings and by the effects of hormones (ACTH and cortisone) need much further study before definite conclusions can be established

Place of entry The place of entry of the rheumatic organism or virus (if such exists) into the body is probably the mouth The faucial tonsils have been considered to be the chief portal partly because their acute infection frequently ushers in acute rheumatic fever and partly because endocarditis may follow tonsillitis directly without any rheumatic symptoms However other lymphoid tissue in the pharynx and nose may also harbor the rheumatic or activating organism and the gastrointestinal tract and foci of infection in sinuses and middle ear have not been ruled out as possible sources of rheumatic heart disease

Rheumatic fever and chorea have been for many years regarded as the chief manifestations of the rheumatic infection that causes heart disease but tonsillitis growing pains and in very young children certain ill defined fevers or illnesses have been thought to be allied as lesser and somewhat uncertain evidences of the same infection The separation between these definite entities of rheumatic fever and chorea and the indefinite infections or symptoms mentioned and between the latter and distinctly nonrheumatic diseases is ill defined in our present state of knowledge the borderline must be regarded as very wide Thus the diagnosis of a rheumatic infection or of rheumatic endocarditis or heart disease still often remains a matter of opinion Two generations ago as now it was rather the custom to consider all infectious heart disease in young people that was not of syphilitic or of malignant bacterial nature to be rheumatic in origin One generation ago there arose the belief that septic infection of nonrheumatic type was frequently responsible when a rheumatic history was not obtainable Probably the truth rests somewhere between these views namely that the large majority of cases of infectious endocarditis are rheumatic in origin but that some arise from other infections particularly terminal in nature even when not of malignant bacterial type

The more carefully one investigates the past history of patients with the rheumatic type of chronic heart disease the more often one discovers a partly forgotten or mild rheumatism or chorea in such patients on the other hand a prejudicial view is inclined to interpret every tonsillar infection or muscle ache as rheumatic Furthermore rheumatic fever does not frankly appear as such in the first few years of life except in rare instances children affected with chronic endocarditis following some poorly defined illness in the second or third year of life are likely later to develop definite chorea or rheumatic fever with recurrent infection of the heart It is safest to regard and to treat as rheumatic all infectious heart disease of childhood (unless it is malignant bacterial endocarditis) even though occasionally the cause is not clearly the rheumatic infection the term rheumatic type of heart disease acute sub-

acute or chronic covers satisfactorily, for the present at least the cases of doubtful etiology

A definite history of rheumatic fever, mild or severe can on careful investigation be found in 60 to 70 per cent of cases with 'rheumatic heart disease and in another 5 to 10 per cent a history of chorea without rheumatism is obtainable Chorea alone with no evidence of infection is not so often followed by heart damage (Jones and Bland 1935) earlier opinions to the contrary were based on failure to exclude infection particularly rheumatic fever

Sex Rheumatic heart disease attacks both sexes, but statistical analysis usually shows a more frequent incidence among females in the ratio of about 4 to 3 or 5 to 4 In one group of 956 cases there were 525 females and 431 males (White and Jones 1928) and in another group of 1 000 cases studied at the House of the Good Samaritan in Boston there were 709 females and 291 males, a 7 to 3 ratio but the preponderance of beds available for females accounts partly for this high ratio (Jones and Bland 1942)

Age In communities where rheumatic heart disease is common it is found in the great majority of cases between the ages of 4 years and 50 years It rarely begins in the first four years of life and is especially rare before the age of two years A case of intrauterine rheumatic heart disease has however been reported (Kissane and Koons 1933) also a case in an infant aged only 17 months has been noted (Schwarz 1932)

Most recently a group of 26 very young children with active rheumatic fever has been reported by Logue and Hurst (1951) of these 26 10 were under the age of four there being 3 three years old 5 two years old and 2 one year old there were also 9 who were four years old in this group 6 who were five years old and 1 whose exact age at the onset of rheumatic fever was not known but who was under five years of age Despite such exceptions long experience has shown that as a rule rheumatic heart disease begins between the ages of 4 and 15 years with height of onset between the seventh and eighth years It has been found that about 1 to 2 per cent of the school children in parts of the United States and Canada where rheumatic fever is prevalent have rheumatic heart disease varying greatly however from place to place or from one part of a city to another (from less than 0 5 per cent up to 4 or 5 per cent) largely dependent on the degree of crowding of living conditions (Robey 1927 Keith and Pequegnat 1947 Quinn 1948) Although some cases develop relatively late that is after the twentieth year of life this is distinctly unusual The mortality beginning in the first decade increases steadily and is highest in the second and fourth decades when infections (especially recurrent rheumatism) and heart failure take their toll Occasional instances of survival to the age of 70 years and a few even to 80 or over (White and Bland 1941) are seen when the cardiac damage has not been extensive The prevalence of rheumatic heart disease (*chronic as well as acute*) by decades in the New England group of 956 cases already noted (White and Jones 1928) as compared with that of 684 cases analyzed 25 years later (White 1951) was as follows

Race All civilized races and nationalities appear susceptible to rheumatic heart disease although a somewhat lower incidence has been noted in China than in parts of Europe and America of the same latitude In New England people of English Scotch Irish Scandinavian French Polish Jewish German Italian and Negro stock have all been found with rheumatic heart disease

Table 6

AGE GROUPING OF CASES OF RHEUMATIC HEART DISEASE IN NEW ENGLAND

Ye s	*Group of 956 Cases Repo t d n 1928*		*G ot p of 684 Ca es Reported n 1951*	
	Cases	*Percentage*	*Cases*	*Percentage*
0–10	116	1 1	53	7 7
10– 0	299	31 3	2 3	3 6
0–30	135	14 1	71	10 4
30–40	165	17 3	91	13 3
40–50	1 3	1 9	102	14 9
50–60	78	8 2	89	13 0
60–70	35	3 6	38	5 6
Over 70	5	5	17	2 5
Total	956		684	

Climate Climate appears to be an important factor in the incidence both of the rheumatic infection and of the rheumatic type of heart disease The colder wetter parts of the temperate zone particularly favor these conditions as do also the colder and wetter seasons of the year—winter and spring in New England autumn and winter in old England In the northern part of the United States the rheumatic infection and its permanent involvement of the heart are five times more frequent than in the southernmost part of the country or in the Philippine or Hawaiian Islands while in the midzone the incidence is between these two extremes For example in Boston at the Peter Bent Brigham Hospital the incidence of rheumatic fever in the years 1914 to 1923 was 1 85 per cent of all medical admissions the clinical incidence of mitral stenosis was 3 89 per cent and the incidence of mitral stenosis in the autopsy room was 4 68 per cent while in New Orleans at the Charity Hospital these percentages from 1916 to 1923 were 0 03 0 08 and 0 23 respectively and in Baltimore at the Johns *Hopkins Hospital from 1914 to 1922 0 73 2 01 and 1 30 re* spectively (Harrison and Levine 1924) This climatic difference has been so great that victims of the rheumatic infection have been advised sometimes to move from northern latitudes to southern and a few have done so the reports from such a step have been in the main favorable (Coburn 1931 Jones White Roche Perdue and Ryan 1937) but it is to be noted that rheumatic heart disease has been discovered in recent years even in natives of tropical lands such as Cuba (Perez de los Reyes et al 1944) Puerto Rico (Francisco 1947) Panama (Hardgrove et al 1946) Curaçao (Hartz and Van der Sar *1946)* and New Guinea (Levine *1946)* Edstrom *(1944)* has even tried to influence the rheumatic infection by artificially producing a

tropical climate indoors in the temperate zone for long time treatment of active rheumatism with suggestive but not conclusive favorable results The Rocky Mountain states harbor a considerable amount of rheumatic heart disease up to 27 per cent of all cardiac patients (Cannon, 1946) as was confirmed by military experience during World War II while the high plateau and perhaps even the lower lands also in Mexico have shown a surprisingly great number of rheumatic heart cases some 30 to 50 per cent of all cardiacs (Chavez 1942 Cortes and Villarreal 1947) It is likely that both prevalence of hemolytic streptococcus infection and overcrowded living quarters play an important role in these areas

Family incidence One of the most interesting features of the rheumatic infection and of the rheumatic type of heart disease is their occurrence in different members of one family Several studies have indicated that from 3[illegible] to 50 per cent at least of patients with rheumatic fever, chorea or rheumatic heart disease have near relatives with a history of similar trouble (as compared to a control series) Three factors are probably responsible for such family incidence (1) inherited susceptibility to the rheumatic infection (2) close contact with the actual spread of the exciting organism from one throat to another and (3) crowded or unsanitary living conditions sometimes with inadequate food and clothing

Social and economic status An important factor in the occurrence of the rheumatic infection and of rheumatic heart disease appears to be the social and economic status of the individual These diseases are much more common by 100 per cent at least among the crowded poor than among the well-to-do inhabitants of almost every community In the large American private schools rheumatic fever chorea and rheumatic heart disease are infrequent while in the large public schools they are relatively common Crowding exposure to cold and wet without sufficient protection malnutrition and fatigue are probably all factors in producing this contrast

Epidemic form Finally there is some evidence that at times under suitable conditions the rheumatic infection in the nature of rheumatic fever assumes an epidemic form This was noted among the soldiers during World War I and infrequently among civilians since and was encountered again in World War II It may occur when an infecting organism of unusual virulence attacks a group of susceptible individuals exposed to adverse conditions such as bad weather and fatigue It has been especially noted in groups of young people immediately following infection by a virulent hemolytic streptococcus in epidemic form a certain number of susceptible individuals though a small percentage of the persons attacked by the original infection may develop rheumatic fever In camp barracks and other living quarters of military personnel during World War II about 4 to 5 per cent of the young men exposed to and infected by the hemolytic streptococcus of various strains developed rheumatic fever some 10 to 15 days later this was especially noted among the new recruits and in more crowded living conditions and in colder climates (Feasby 1944 and Barber 1946)

Pathology A generation ago endocarditis was the only well recognized common manifestation of rheumatic heart disease acute or chronic pericarditis was admitted as an occasional complication but little attention was paid to involvement of the myocardium or as a matter of fact to the widespread effects of the disease throughout the body Much advance in the proper understanding of this kind of heart disease has come in the last thirty years

The more severe the rheumatic infection in early youth the more extensive as a rule is the cardiac damage Once it was thought that only about two thirds of the attacks of rheumatic fever and about one third of those of chorea affected the heart but careful examination is now revealing a somewhat different incidence There was for example evidence of permanent cardiac damage in 86 per cent of 518 cases of rheumatic fever in 73 per cent of 348 cases of chorea and rheumatic fever and in 3 per cent of 134 cases of uncomplicated chorea analyzed at the House of the Good Samaritan in Boston (Jones and Bland 1935) Findings vary however as indicated by another series of 175 cases of acute rheumatic fever 50 per cent of whom showed no evidence of heart disease after follow up periods averaging seven years (Brown and Wolff 1940) Electrocardiographic and postmortem examinations have often shown myocardial and even slight endocardial involvement even though on physical examination there had been no sign whatsoever of heart disease It is probable that in every case of rheumatic infection there is some heart disease however slight or transient and that in a certain percentage of the total number there is complete recovery with return to normal or at least not sufficient deformity of valves or lesion of myocardium or pericardium to produce abnormal signs

The typical heart lesion of the rheumatic infection is an inflammatory reaction about the smaller arteries consisting of groups of small round mononuclear cells with a few giant cells (Aschoff 1904) this has been called the Aschoff body (Figure 82) and its discovery anywhere in the heart or pericardium has been considered almost pathognomonic of the activity of the rheumatic infection There may be but few of such lesions present or they may be widespread and in groups They apparently come and go leaving no trace unless the disease has been so extensive that nutrition has been interfered with and scar tissue results a sequela of more than slight fibrosis is very rare in the myocardium although a few instances have been recorded of rheumatic heart block remaining as a chronic state after it has appeared during the acute rheumatic infection

Aschoff L Zur Myocarditisfrage *Verhandl d deutsch path Gesellschaft* 1904 VIII 46

Aschoff here gives the first clear description of the more or less specific rheumatic myocardial lesion which has been called by his name (Aschoff body) (The translation is by myself)

We have succeeded in establishing the histological structure of the myocardial reaction to the rheumatic infection by finding peculiar nodules which appear to be specific These nodules were indeed clearly defined in only two cases of recurrent endocarditis but in other cases cellular proliferations corresponded exactly in

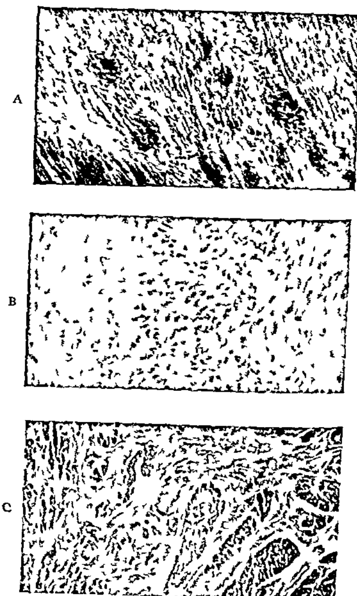


FIG 82 Rheumatic myocarditis (*A*) Microphotograph showing typical Aschoff bodies in the (ventricular) heart muscle in acute rheumatic heart disease (Thalhimer and Rothschild *J Exper Med* 1914 XIX 417)

(*B*) Microphotograph (higher power) of myocardium of child dying of severe rheumatic infection showing extensive destruction of the muscle cells with invasion by leukocytes and a few multinucleated giant cells (Kindness of the House of the Good Samaritan Boston)

(*C*) Microphotograph of myocardium from case dying of severe recurrent rheumatism There is evident at the left old fibrotic change from a previous rheumatic infection, and at the right new necrotic and hemorrhagic lesions due to the recurrent rheumatism (Kindness of the House of the Good Samaritan Boston)

their locations to the lesions of these two hearts They were regularly situated in the neighborhood of the small and medium sized blood vessels and often showed the closest relationship to the adventitia of these vessels There even was found a disease of all the vessel walls somewhat comparable to that described for arteritis nodosa The above mentioned nodules are extraordinarily small highly submiliary and are comprised of collections of unusually large cells with one or more ab-normally large slightly notched or polymorphic nuclei The grouping of cells often occurs in the form of a fan or a rosette The periphery of the nodule is composed of the large nucleated cells and the center often of an apparently weakly staining necrotic mass of coalescent cellular protoplasm With careful observation the fan shaped foci remind one of the smallest necrotic areas with cellular periphery which one finds so often in gouty kidneys In the rheumatic nodules one has to do not with the tubercular or foreign body giant cells with several regularly formed nuclei but with structures which resemble rather the large nucleated cells in certain sar comas or in pseudoleukemic proliferations On the other hand the nodules are not composed solely of such large nucleated cells but small and large lymphocytes and also polymorphonuclear leukocytes are wedged in between the large cells at least at the periphery or else themselves comprise an outer zone from which irregular stray cells extend out further into the connective tissue interspaces In these outer areas there can still be found single large nucleated cells and all gradations down to simple large leukocytic elements which are more or less commonly found in the neighborhood of the smallest vessels in all inflammatory reactions These leuko-cytic elements are the large cells which Hayem and Romberg have described but whose origin remained doubtful in their minds Out of these large cells which are the adventitial cells of the blood vessels swollen by inflammatory reaction the large nucleated giant like cells are formed which single or collected in nodules give to the rheumatic proliferations a characteristic stamp It should further be observed that the number of eosinophilic cells in these nodules is very small

Years later it was demonstrated that the Aschoff body is not the earliest tissue change in the rheumatic infection but often is a rather late reaction probably a part of the process of recovery and repair (Coburn 1933) The earliest tissue changes are those of destruction (necrosis) and a tendency to hemor rhage throughout the body especially well marked in the more severe cases The myocardium particularly is involved and may be so seriously damaged in the sicker children that the heart dilates acutely or subacutely Such dilatation of the heart may lead to death from heart failure or to more or less permanent cardiac enlargement or it may be followed by good recovery with more or less complete return of the heart to normal size The recognition of this fact is of the greatest importance in the proper understanding of the cardiac symp-toms and signs in the course of the acute and subacute rheumatic infection in the analysis of the late after-effects and in rational prognosis and treatment

The typical rheumatic endocarditis consists of a so-called verrucous inflam matory reaction tiny vegetations of thrombotic nature composed chiefly of fibrin and tending particularly to appear in a row on the atrial surface of the mitral and tricuspid valve cusps and on the ventricular surface of the semi-lunar valve cusps (Figure 83) at the line of closure not at the edge although

sometimes they are distributed elsewhere over the cusps The exact pathogenesis of these thrombi or of the damaged areas of the endocardium on which the thrombus formation takes place is not known whether due to direct toxic action of the blood stream or via the blood vessels in the valves or to local allergic reaction to agent or agents in the blood (manufactured elsewhere) In any event the slight trauma caused by valve closure appears of some importance in favoring the appearance of the earliest lesions In fact nonrheumatic



FIG 83 Photograph showing acute and chronic rheumatic endocarditis of the aortic valve Note the vegetations along the line of closure adhesions of the cusps to produce slight aortic stenosis scarring of the endocardium below the valve and thickening of the chordae tendineae of the mitral valve The patient was a boy 14 years old (Kindness of Dr Ronald Grant Guy s Hospital London)

bland thrombi of small size very probably are deposited on the lines of closure of the heart valves especially the mitral on occasion almost as a normal event the result of a variety of influences they may do no serious harm but can quite likely result in a slight chronic thickening of the valve edge which may justifiably or not arouse suspicion of a rheumatic etiology Besides the involvement of valve cusps there is commonly in rheumatic endocarditis especially of the severe type inflammation of the chordae tendineae and of the wall of ventricle or atrium especially of the left atrium just above the valve this results in scarring and in the case of the chordae in thickening shortening and coalescence to add to the valve deformity

Rheumatic pericarditis consists of a fibrinous or a serofibrinous reaction more or less extensive sometimes giving rise to the typical bread and butter appearance (as shown in Figure 134 page 710) but rarely to large effusions (a typical serous exudate rarely bloody) In healing small or large scars are left with or without localized or complete adhesions and only rarely with any important external adhesions Constrictive pericarditis of sufficient degree to cause symptoms or signs (Pick s disease) has not been encountered once in 1 000 cases of the rheumatic infection many with pericarditis followed over a ten to twenty year period at the House of the Good Samaritan in Boston (Jones and Bland 1942) nor has any one of 53 cases of chronic constrictive pericarditis examined by myself had a rheumatic etiology although two among them had coincidental rheumatic valvular disease

When as frequently happens myocardium endocardium and pericardium are all involved we speak of *pancarditis* and now and then especially in young children such pancarditis may be very severe and overwhelming resulting in early death from heart failure

Furthermore the rheumatic infection may attack other organs beside the heart, pericardium joints and brain (chorea) The arteries—aorta pulmonary artery and smaller visceral and peripheral vessels—the lungs the pleurae the diaphragm and the peritoneum may be involved by hemorrhages or by lesions resembling the Aschoff body sometimes with serious consequences An important and interesting pulmonary rheumatic lesion in severe cases is the hemorrhagic consolidation sometimes labeled erroneously rheumatic pneumonia this lesion quickly comes and goes

The rheumatic infection is typically a slow one and recurrent a fresh invasion of the heart is common on top of healed lesions of valves or of atrial or ventricular endocardium of chordae tendineae or of pericardium

The infection may clear up in some cases as stated above with little or no trace but commonly a scarring of the endocardium is made evident by valvular deformity Chronic pericardial damage sometimes persists in the nature of adhesions of varying extent and importance Rarely there is a residual myocardial lesion as shown by permanent heart block or ventricular dilatation A discussion of the particular valve lesions of pericarditis and of heart block will be found in Parts III and IV of this book Suffice it to say here that there is a very wide variation of cardiac damage resulting from the rheumatic infec

tion and constituting chronic rheumatic heart disease not only with respect to the particular parts of the heart involved but also with respect to the degree of involvement

It should be added that chronic cardiac dilatation accompanying valvular defects or pericardial adhesions may be due as much or more to the rheumatic infection of the myocardium as to the particular valvular handicaps that cause heart strain Indeed it may be conjectured that in rare cases cardiac enlargement even of high degree and leading to failure may be due to an old severe antecedent rheumatic involvement of the myocardium with little or no endocardial or pericardial scarring This is an explanation of some of the cases of heart disease of unknown origin which appeals to one as logical but which as yet lacks proof

Symptoms The symptoms of rheumatic heart disease depend upon three factors (1) activity of the rheumatic infection (2) obstruction to the circulation resulting from the specific lesions and (3) heart failure which may come as the result of overwhelming acute or subacute myocarditis or of chronic valvular disease or of disturbed heart rhythm or of two or even *all three* of these conditions combined Many persons with chronic rheumatic heart disease have no symptoms at all and live active lives without difficulty Of greater immediate importance than study of the structural defects is the determination of the presence or absence of activity of the rheumatic infection

The symptoms of acute or subacute rheumatic infection include those of any infection but depend also on the reaction of the individual patient to the causative agent Joint pain tenderness swelling heat and redness muscle aching chorea (rarely combined with joint symptoms) fever chills (rarely) sweating (sometimes profuse) weakness effort syndrome malaise anorexia epistaxis (occasionally), and loss of color and weight are all symptoms of the active rheumatic infection Their severity varies with the virulence of the infection and the resistance of the patient They may be mild and hardly noticeable —merely slight fever and malaise with or without muscle or joint soreness— and not always sufficient to cause the victim to stop school or work or to induce the family to consult a physician unless they have been educated by previous experience or are aware of the likelihood of involvement of the heart In rare cases of rheumatic fever there may be abdominal pain simulating that of or actually due to an acute appendicitis A low grade rheumatic heart infection ordinarily called subacute rheumatic carditis may set in and last for weeks or months or even years especially in children showing itself only by a loss of energy and by the appearance of ill health and of a slight elevation of temperature at intervals or daily (99° F or a little more by mouth or 100° F by rectum) Such a situation is very common while a virulent polyarthritis in children is relatively rare A severe short attack of rheumatic fever with extreme joint involvement and little or no heart disease is much more likely to occur in the adult Years ago it was a common though by no means invariable rule that the older the individual the more the joints suffered and the less the heart the younger the subject the more the heart suffered and

the less the joints In recent years on the other hand a fulminating poly-articular rheumatism is rarely seen at any age even in New England this is apparently due to a spontaneous change in the virulence or character of the rheumatic infection itself though the common and early use of the salicylates (especially aspirin) for any illness by the populace at large may also have a modifying and misleading influence on the acute rheumatic process

The heart itself when acutely invaded by the rheumatic infection only occasionally causes symptoms Sometimes it may ache so that precordial dis comfort is felt sometimes there are sharp pains in the chest although they are not common rarely there is actual angina pectoris occurring usually in subacute or chronic valvular disease with marked aortic regurgitation prob ably dependent on insufficient coronary blood supply due not only to low diastolic blood pressure but also to a storm of vasoconstriction involving the coronary arteries and producing transient hypertension in a sensitive indi vidual Infrequently disturbances of rhythm occur such as premature beats or paroxysmal tachycardia giving rise to palpitation usually the palpitation that may be felt is but a part of the effort syndrome that accompanies any infection Dyspnea also is usually due to effort syndrome but sometimes it arises from an acute pericarditis or from cardiac dilatation and failure accom panying an overwhelming acute myocarditis When the heart fails during the acute rheumatic infection in childhood it is a total heart failure with little or no dyspnea but with congestion behind the right ventricle giving rise on occasion to upper abdominal discomfort from engorgement of liver and other abdominal viscera

The chronic rheumatic heart frequently fails from the strain of valvular disease complicated by a disturbing arrhythmia (especially atrial fibrillation) or by an acute infection (rheumatic or nonrheumatic) then appear the typical symptoms of congestive failure (see Chapter 30) Angina pectoris may occur with marked aortic stenosis or regurgitation but rarely with other valve defect Also without actual failure the obstruction due to mitral stenosis may occa sion congestion of the lungs with dyspnea cough hemoptysis or it may rarely cause hoarseness from laryngeal paralysis At times the obstruction due to tricuspid stenosis may block the return of blood into the right ventricle and left heart chambers with resulting congestion of liver and large veins similar to the condition found in cases of chronic constrictive pericarditis (so-called Pick s disease)

The symptoms of an active rheumatic infection may frequently be super imposed on those of chronic rheumatic heart disease when there is a recurrent rheumatic attack in fact heart failure in chronic rheumatic heart disease is often precipitated by the new infection or is due more to its presence than to the old lesion

Signs The signs of rheumatic heart disease are dependent on the factors of activity of the infection of the strength of the heart and of the particular lesions There may be nothing but slight enlargement of the heart with a systolic murmur at the apex or a slight diastolic murmur along the left border

of the sternum found on routine examination there may be an enormously enlarged heart with several murmurs absolute arrhythmia and marked congestive failure or there may be any combination of signs between these two extremes Commonly in the child there is slight to moderate cardiac enlargement with normal rhythm moderate systolic and middiastolic murmurs at the apex (the result of left ventricular dilatation during the course of the first rheumatic infection and later on, of mitral valve disease itself) and sometimes a diastolic blow (of aortic regurgitation) *along the left border of the sternum* without frank congestive heart failure but frequently with slight fever due to activity of the rheumatic infection It is a common experience to note the disappearance of the physical signs of rheumatic heart disease (enlargement, systolic murmur and even mitral diastolic murmur) when cardiac dilatation subsides along with the active rheumatic infection (Bland Jones and White 1936) *these signs especially the mitral diastolic murmur used to be attributed* to chronic heart disease but now it is realized that usually an interval of several years is necessary for the establishment of structural mitral stenosis Commonly in the adult on the other hand especially in the female there is a well marked apical diastolic murmur of mitral stenosis, absolute arrhythmia of atrial fibrillation and very limited cardiac reserve or slight to moderate congestive failure with or without aortic regurgitation in the adult male one finds somewhat more often a preponderant or even seemingly isolated aortic valve lesion (stenosis, regurgitation or both) with normal rhythm Although these findings are the most common they may be replaced by others The signs of the particular valve defects will be discussed in Part III

The more severe cases of active rheumatic infection may show also frank congestive heart failure which in childhood involves the whole heart with resultant systemic venous congestion (big liver and dependent edema including the face with the child lying flat) rather than pulmonary congestion due to primary left heart failure (Walsh and Sprague 1941)

Infrequently one finds in acute rheumatism two additional signs which are subcutaneous and cutaneous manifestations rheumatic nodules and skin lesions

Rheumatic nodules are important signs of a severe rheumatic *infection* their presence indicates that the infection is still active even though they persist or recur for many months These nodules vary in size number location and with the severity of the disease Usually of pinhead to pea size and shape rarely as large as Lima beans they are found most commonly subcutaneously and are loosely attached to tendon sheath periosteum or joint capsule over *elbows knees ankles skull fingers wrists toes and shoulders* in frequency in about the order named and usually more or less symmetrically on the two sides of the body (Figure 84) When very extensive they may be found scattered over the entire head thorax and long bones In number they vary from two or three a common finding to one hundred or more very rarely They tend to come and go singly or in crops each one lasting for a few days or weeks they may not completely disappear for months In some parts of the

world they are more common than in others but this variation is probably due mainly to the severity of the infection Their incidence has extended from 2 or 3 per cent to over 75 per cent in different groups of patients with acute rheumatic infections in different communities They are less commonly seen nowadays in New England than they were two or three decades ago perhaps paralleling the decrease in the severity of the disease itself

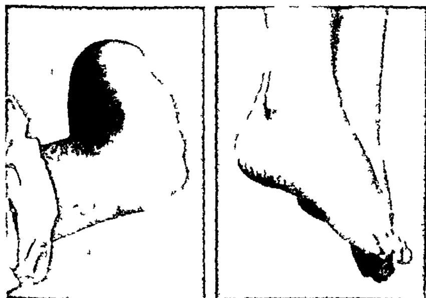


FIG 84 Photograph showing joints of child with rheumatic nodules on elbow ankle and foot Note nodule also on the tendo Achillis (Kindness of the Cardiac Clinic Children s Hospital Boston)

Erythema multiforme (marginatum) is the commonest of the cutaneous signs accompanying the rheumatic infection occurring in about 15 per cent of the cases at some time or other tending to recur over periods of a few weeks or months and to appear in patients who have had or who later develop rheumatic nodules Erythema nodosum urticaria and angioneurotic edema are relatively rare Purpura rheumatica and petechial hemorrhages are some times found Petechiae may be readily produced in the skin of subjects with an acute or subacute rheumatic infection by pressure as with a blood pressure cuff this is due to the tendency to bleed which is a part of rheumatic fever as well as of bacterial endocarditis

Other occasional signs of severe rheumatic infection are those of acute pleuritis acute pericarditis or both fibrinous or with effusion and sometimes hemorrhagic pulmonary disease (areas of hemorrhagic consolidation) which are apparently of rheumatic origin and as a rule rapid in their appearance and disappearance Chronic adhesive pericarditis may show itself in the recovered cases but often it gives no clear sign This will be further discussed in Part III of this book

The results of all other methods of examination of an individual with rheumatic heart disease are likewise dependent on the three factors of activity of infection cardiac insufficiency, and the particular structural lesion Commonly it is the presence of mitral valve disease and of stenosis of that valve that accounts for the findings in chronic cases

The blood pressure is normal or low unless there is a complicating essential hypertension thyrotoxicosis, or considerable aortic regurgitation The pulse and pulse pressure are very full when there is marked aortic regurgitation small when there is considerable mitral stenosis and very small when there is pronounced aortic stenosis

Roentgenologic study is of help in following a case of rheumatic heart disease In the acute infection and early stages of organic involvement the heart shadow may be normal or it may reveal enlargement and change in shape of the heart shadow due most often to more or less acute dilatation of the heart (Figure 85) or less commonly to accumulation of fluid in the pericardium in rheumatic pericarditis or to both of these conditions In chronic cases it shows various typical changes of shape and size when there are well marked chronic valvular lesions (see Chapter 26)

The electrocardiogram may be normal in rheumatic heart disease except for a rapid rate (sinoatrial tachycardia) which is found frequently, but if many serial records are taken of any case abnormalities are commonly found though often in but a few records When the electrocardiogram is abnormal it may show either an arrhythmia delay in conduction between atria and ventricles abnormal *T* waves intraventricular block or abnormal axis deviation The rhythm is absolutely irregular in more than half of the adult cases with marked mitral stenosis but it is generally normal or disturbed only by premature beats in aortic valve disease, pericarditis or preponderant mitral regurgitation Slight grades of heart block as shown by *P-R* intervals of 0 21 or 0 22 second are common during the acute rheumatic infection (Figure 86) and even *P R* interval prolongation to 0 25 second dropped beats or higher grades of block are occasionally seen This finding of block may be the only sign of cardiac involvement and it has been noted in rare cases as the first evidence of the rheumatic infection in the body polyarthritis developing shortly afterward (White 1916) Also in very rare cases the heart block during the active infection may progress to such a high degree that Adams Stokes attacks occur for a short time As a rule the heart block clears up when the rheumatic infection subsides but a few instances of permanent rheumatic heart block have been noted and it has also been observed that rheumatic heart cases with a persistently prolonged *P-R* interval are more likely to develop atrial fibrillation than are those whose *P R* interval is normal due in part it is suggested to vagal action (Bruenn 1937 Altschule 1939) It is important to note moreover that prolongation and variability of the *P R* interval can occur in normal children as well as in rheumatic children without evidence of rheumatic activity (Reyersbach and Kuttner 1940)



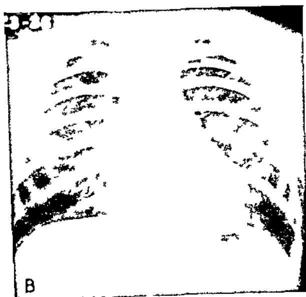


FIG 85 Roentgenograms showing (*A*) considerable dilatation of the heart in a young girl during acute rheumatic fever and (*B*) reduction in heart size several months later after complete subsidence of the infection At the time the first record was taken there were systolic and middiastolic murmurs at the apex which disappeared wh n the dilatation subsided There was no evidence of acute pericarditis Note the rather localized pulmonary edema in the right lung in (*A*) The transverse diameter of the heart in (*A*) was 11 6 cm and in (*B*) 10 4 cm

In addition to the delay in atrioventricular conduction slight deformities of the *QRS* and *T* waves or of the *S-T* segment are occasionally noted during the acute and subacute infection and may represent slight transient intra ventricular block myocarditis and pericarditis, rarely they may persist In a few cases of chronic rheumatic heart disease particularly with mitral stenosis bundle branch block of the right type with wide S_1 or QS_1 may be

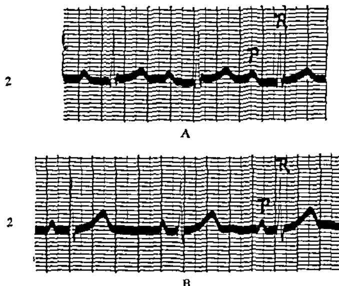


FIG 86 Electrocardiograms showing Lead 2 in (*A*) during acute rheumatic fever Dec 17 1935 and in (*B*) two weeks later during convalescence Jan 2 1936 Note the prolonged *P R* interval (0 25 second) in (*A*) and normal *P R* interval (0 17 second) in (*B*) Boy 13 years old Time = 0 1 and 0 2 second

found Finally it is common to find abnormal axis deviation and ventricular preponderance in chronic valvular disease if either mitral stenosis or aortic regurgitation is preponderant and of marked degree right axis deviation occurring with the former and left axis deviation with the latter Absence of abnormal axis deviation by no means rules out either valvular lesion in fact high degrees of both may be present in the same case with normal electric axis deviation the effect of involvement of one of the valves neutralizing the effect of involvement of the other in the classical limb leads but the precordial *leads reveal the enlargement of both ventricles A very interesting* electrocardiographic finding occasionally seen in acute rheumatic fever with congestive heart failure is a shift of the electric axis to the right due doubtless in large part to the acute right ventricular dilatation (more marked than that on the left side) which decreases or disappears with the patient's improvement or recovery (Walsh and Sprague 1941) Prolongation of the *Q T* time has been reported in rheumatic fever but it is not a consistent finding and may be due to other factors (e g cardiac enlargement) rather than to the rheumatic fever itself

Blood and urine are frequently abnormal when there is an *active* rheumatic or complicating infection or congestive failure A leukocytosis of 10 000 or over often but not always accompanies acute rheumatic heart disease the severer the infection the higher the white count but it rarely passes 20 000 A slight or even moderately severe hypochromic anemia is common in children with active rheumatic heart disease The sedimentation rate of the blood is usually increased in proportion to the activity of the rheumatic disease and may be the only evidence that persists of a long-drawn out low grade infection The blood culture is usually negative A positive skin re action has been reported as a frequent finding when the toxic filtrate of the hemolytic streptococcus (or its nucleoprotein) is injected intradermally in patients who have had rheumatic fever but this has been found to be a non specific reaction that is it occurs also in cases who have had Streptococcus hemolyticus infections without rheumatic fever Albuminuria is the usual finding during congestive heart failure and during moderate or high fever in the acute rheumatic infection Occasional red blood corpuscles are frequently found in the urinary sediment during the active infection

Course and prognosis Rheumatic heart disease begins with an acute in vasion of the heart generally in childhood between the ages of 4 and 12 years Instances of very early infection are on record even in the fetus and in the nursing infant whose mothers had rheumatic fever at the time on the other hand the rheumatic infection and resulting heart disease have sometimes occurred *first in* adult life initial attacks of rheumatic fever have been reported in six patients over 60 years of age (Ferris and Myers 1935) I have myself encountered cases with recurrent attacks at 66 and at 72 years of age The earlier in life the cardiac involvement the more serious it is likely to be and the shorter the patient s life It is usual for the child to survive the first rheumatic infection whether it is frank rheumatic fever chorea ill-defined sickness or rheumatic heart infection alone Although this earliest infection is often mild it may last for months or years and leave a badly crippled heart Recurrent infections throughout childhood may cause death by heart failure by the toxic effect of the disease itself or by complications But usually there is survival in spite of one two three or more fresh attacks or exacerbations of rheumatism in childhood and youth the victim showing a variable amount of permanent heart damage by the time he reaches the age of 20 years Rarely does he escape unscathed unless he has had but one or at most two slight attacks of rheumatism The greater the number of recurrences of the infection the greater is the heart damage In adult life he runs far less risk from new rheumatic attacks but on the other hand he runs three other risks (1) atrial fibrillation (2) congestive heart failure and (3) subacute bacterial (Streptococcus viridans) endocarditis The first of these complications (atrial fibrillation) is common in the case of well marked mitral stenosis but it is relatively rare in all other cases The second (congestive failure) is likely to occur in any severely damaged heart when there is aortic or mitral valve disease uncontrolled tachycardia (especially in atrial fibrillation)

infection rheumatic or otherwise which adds appreciably to the strain The third (subacute bacterial endocarditis) is commonest in aortic valve disease or with mitral lesions in which stenosis is not marked that is when regurgitation predominates so it is most common in just that type of chronic rheumatic heart disease which atrial fibrillation and congestive failure are not likely to accompany but why this should be so we do not yet know

Death from heart failure or complicating infection commonly overtakes the victim of rheumatic heart disease in the second fourth or fifth decade of life after many years usually ten to twenty of partial crippling and restriction of activity and after a few years usually two to five of partial or complete invalidism Sometimes however if the lesions are but slight and the subject is careful fortunate or both he may survive to old age and die a noncardiac death Slight mitral stenosis or regurgitation slight aortic stenosis or regurgitation and a noncrippling adhesive pericarditis are all lesions that are well borne with respect both to duration and to activity of life but in general the mitral valve lesions are better borne than the aortic A ten year follow up of 506 cases with rheumatic valvular lesions gave a relative mortality of 3 7 per cent for mitral insufficiency, 12 5 per cent for mitral stenosis and 37 4 per cent for aortic valve lesions with or without mitral valve involvement (Svartz and Ernberg 1947) In Texas Fashena (1944) found the death rate from rheumatic fever in the school age period to be not very different from that in New England or in the United States as a whole Cases of mitral stenosis surviving the age of 80 years are now on record (White and Bland 1941) Wilson and Lubschez (1948) have presented some interesting data as to longevity based on a thirty year period of observation of 1 042 children who had rheumatic fever The mean age at onset of their rheumatism was 6 5 years The average length of observation was 14 8 years among 226 deaths 75 7 per cent were due to rheumatic disease of the heart and 10 2 per cent to subacute bacterial endocarditis They concluded that an affected child has 4 chances out of 5 to survive childhood 3 out of 4 to survive puberty and then 19 chances out of 20 to survive early adult life, with an overall chance of 1 out of 2 to survive the age of 40 years

Complications The three most important complications of rheumatic heart disease have been mentioned above (1) atrial fibrillation which complicates two thirds of the cases of considerable mitral stenosis and about one *fifth* of all cases of chronic rheumatic heart disease (17 5 per cent of the 956 cases of White and Jones series) (2) congestive heart failure which eventually complicates at least two thirds of all cases and (3) subacute bacterial (Streptococcus viridans) endocarditis which attacks one in every 4 to 20 cases (25 to 5 per cent) of rheumatic heart involvement Jones and Bland (1942) have found subacute bacterial endocarditis in 16 (7 9 per cent) of 203 fatal cases of rheumatic fever or rheumatic heart disease while Gelfman (1943) has reported the finding of such involvement in 2[illegible] cent of autopsied cases of rheumatic heart disease in two Boston hosp[illegible] common or important complications are co[illegible] disease [illegible] of White and Jones

series) essential hypertension (also in 2 per cent of White and Jones series) syphilitic aortitis congenital defects thyrotoxicosis and emphysema (each of which last named conditions complicated less than 1 per cent of White and Jones series) Neurocirculatory asthenia frequently is found in varying degree in the victim of rheumatic heart disease it was well marked in 37 of the 956 cases (4 per cent) of the series noted above (White and Jones) Mild and serious infections of all sorts nephritis pulmonary disease nervous diseases and lesions of the gastrointestinal tract may complicate rheumatic heart disease but it is of interest to note that glomerulonephritis rarely accompanies rheumatic fever itself (Baehr and Schifrin 1931) The relative infrequency of pulmonary tuberculosis in cases of well marked mitral stenosis has been pointed out it has been suggested that the chronic pulmonary stasis in mitral stenosis protects the lungs from tuberculosis

Four complications of rheumatic heart disease are largely dependent on the mitral stenosis or congestive failure that may be present The commonest is pulmonary embolism which may arise in dilated right heart chambers but most often comes from thrombosed veins in legs resulting largely from the venous stasis secondary to the heart trouble Embolism to brain or elsewhere may result from thrombosis in the left atrium Acute pulmonary congestion producing edema or hemoptysis may come from increased pressure in the pulmonary circulation due to mitral stenosis especially when there is a rapid heart rate Rarely hoarseness may result from left recurrent laryngeal paralysis

Another rare complication namely that of angina pectoris may attend rheumatic heart disease it was found in 13 of White and Jones series of 956 cases the 5 older cases having coronary disease and the 8 younger ones marked aortic regurgitation Angina pectoris may also very rarely complicate mitral stenosis in young people (Hochrein 1930)

Of disturbances of rhythm atrial fibrillation and heart block have been discussed Atrial flutter is rare generally complicating mitral stenosis Paroxysmal tachycardia (regular) is common but less frequent than atrial fibrillation The presence of sinus arrhythmia although somewhat favorable is of little aid in the judgment of a case since it does not indicate that the heart is normal and since it does not prove that a low grade active infection is no longer in progress as was once thought

Treatment No treatment for rheumatic heart disease per se is needed unless one or more of the important complications are present—infection atrial fibrillation or flutter or congestive failure The treatment of the arrhythmias and of congestive failure is discussed in Part IV of this book In prevention of acute rheumatism either in first or in recurrent attacks the most important measure is the avoidance of upper respiratory infections or the early and adequate use of penicillin if the hemolytic streptococcus is the offending agent Although helpful it is not essential to enlist the aid of a mild climate for children have been kept well even in open air sanatoria in the north in the winter by practical exclusion of infected contacts (Hubbard and Griffin 1940)

If acute or subacute rheumatic infection is present *rest in bed*, a light simple diet with adequate vitamins and appropriate therapy directed against the infection are indicated Usually *good nursing care* is of prime importance and worth more than most drugs Satisfactory gain in weight is a good indication of the favorable progress of convalescence but it is not a sign of cure

In the third edition of this book it was stated that for the rheumatic infection itself no specific therapy has as yet been established although much reliance has been placed by some on the *salicylates* which without any question have a well nigh specific effect in the rapid control of fever joint swelling and pain in rheumatic fever for which purpose they may be freely used It is possible also though not proved that salicylate therapy may help to effect a rapid absorption of rheumatic pericardial and pleural exudate and effusion' Since that time hormone therapy of arthritis and certain other diseases including rheumatic fever, has been introduced which may or may not prove to be specific or very near it

Hormone therapy The application of ACTH (adrenocorticotropic hormone) to acute rheumatic fever has been tried recently with surprising immediate success in the majority of cases for example seven patients at the House of the Good Samaritan in Boston given 10 to 25 mg of ACTH four times a day for four to six weeks have all responded favorably As a rule their temperature has been reduced to normal in two to three days their sedimentation rates have become normal in two weeks and even those seriously ill with congestive failure have improved greatly although they still may need other treatment for the congestion itself Cortisone also has been found to be effective in suppressing the disease (Hench et al, 1950) These preliminary observations of course need further confirmation and more prolonged follow up

Salicylate therapy A dose of 15 to 30 gr (1 to 2 gm) of sodium salicylate with an equal amount of sodium bicarbonate every two to four hours until relief of symptoms and of fever or a toxic reaction (tinnitus nausea vomiting urticaria) has ensued is sometimes recommended with great benefit in this way even 150 to 240 gr (10 to 16 gm) may be administered in a single day Rarely is it necessary or possible to continue such a large dosage for more than a few days For children the dosage of salicylate may be halved and for infants one fifth to one tenth of the amount given to adults should suffice but of course this medicine will rarely be needed at such an early age

Intravenous salicylate therapy in large dosage has been tried out controlled by testing the concentration of the drug in the blood (Coburn, 1944), but its early promise like the saturation by oral salicylates a good many years ago has not been confirmed Thus the statements made in the previous editions of this book still hold namely that the antipyretic effect of salicylates if constantly given may conceivably be harmful by masking some of the evidences of activity of the infection and so misleading one into a false sense of security and that if salicylates are used they should be employed only for symptoms of discomfort due to exudative reactions to the disease and occasionally

omitted for a few days at a time to determine the true course of the disease (temperature leukocyte count and signs and symptoms) However in the course of the trial of intravenous salicylate therapy a useful test for blood salicylate content was devised It has been demonstrated incidentally that as high a blood concentration of salicylate can be secured by oral adminis tration as by intravenous Finally a warning is due as to the toxic effects of salicylate poisoning including a tendency to bleed and even delirium—such toxicity is more readily produced by intravenous administration

Vitamin C therapy Apparently midway between the effects of ACTH and salicylates is that of massive doses of vitamin C the favorable effect of which has recently been described by Massell et al 1950 Acute rheumatic involvement has been controlled in a series of cases by the administration of 1 gm of vitamin C in orange or apple juice four times a day The exact mechanism by which this effect is produced is still obscure

No place has been found for antihistaminic drug therapy in rheumatic fever despite the common supposition that this disease may be related to the allergies

Serum treatment of the acute rheumatic infection whether or not the infection involves the heart has never evolved from the experimental stage The use of specific monovalent or polyvalent streptococcus vaccines has also been suggested and tried but further study is needed before definite conclusions can be reached A possible success of such therapy is to be ascribed rather to the reduction of streptococcus infections which may excite the rheumatic infection than to the primary control of the rheumatic infection itself

A much more important prophylactic measure recently introduced that bids fair to reduce the incidence of the rheumatic infection in initial and especially in recurrent attacks has been first the administration of sulfona mide drugs in small dosage routinely throughout the winter and spring to susceptible children (e g 1 0 to 1 3 gm 15 to 20 gr sulfanilamide divided into 2 or 3 doses daily to a child of 8 years) to ward off or in larger dosage to treat the hemolytic streptococcus infections that so often precipitate active rheumatism and heart disease (Thomas et al 1939 1941 1942 Coburn 1941 Hansen et al 1942 and Kuttner and Reyersbach 1943) and more promising still of late the use of penicillin especially at the time of exposure to a streptococcus sore throat or when such is just beginning (Malmer and Amsterdam 1947 Goerner et al 1947 Milzer et al 1948 Massell et al 1948 Denny et al 1950) A daily oral dose of 100 000 to 300 000 units of penicillin has been found apparently effective (Pitt Evans 1950 Massell personal communication 1950) Similar preventive medicine may hopefully be practiced during acute infections or operative procedures (especially dental extractions) in the case of individuals with chronic rheu matic heart disease to ward off subacute bacterial endocarditis We still await however the final word as to the efficacy of these drugs in the prevention both of rheumatic fever and of subacute bacterial endocarditis

It is to be noted that neither penicillin nor streptomycin nor the sulfonamides have any favorable influence on the rheumatic process per se in fact the two latter may cause harm by their toxic effect

The *treatment of chorea* has been no more satisfactory than that of rheumatic fever Absolute rest and quiet, with good nursing care are more effective than any other measures Neither arsenic (e g Fowler s solution) nor the salicylates nor other drugs or serum appear to have any specific action in controlling chorea except for a promising recent experience with hormonal therapy (adrenocorticotropic hormone) For very severe (convulsive) chorea magnesium sulfate intramuscularly, intravenously or intraspinally (in 25 per cent solution) has been reported to have a sedative effect Phenobarbital (Luminal) barbital (Veronal) or other mild sedatives tincture of stramonium and continuous baths have also been recommended Febrile therapy by the use of foreign protein such as typhoid vaccine has also been used but this as a matter of fact may do harm by inciting an attack of rheumatic fever (Bland and Jones 1935)

The *convalescent care* of patients suffering from subacute rheumatic infections long continued and lasting for weeks months or even years has been a problem attracting much attention in recent years It is generally agreed that the active stage of the infection should be treated by rest in bed but there comes a time when it is difficult or impossible to be sure whether or not the infection has completely subsided In the case of restless children who feel well enough to run about and whose control is difficult at home much discretion must be used for such cases institutional care where the discipline is *good or supervision by able nurses may be essential during the active stage* of the infection When with the patient at rest in bed and not taking salicylates the temperature no longer rises over 99° F by mouth or 100° F by rectum the leukocyte count remains below 9 000 the sedimentation rate becomes normal the pulse rate keeps under 100 symptoms and signs of infection have disappeared and the nutrition is improved convalescence may be considered to have begun The further length of time after that during which rest in bed should be continued and the rapidity at which convalescence should be allowed to proceed to full normal activity should not be determined by any set rule (some have been suggested) but by the conditions in the individual case After severe infection a minimum of several months of convalescence should be prescribed before return to normal activity during this period a foster home or preferably the child s own home should be utilized with training of the family to cope properly with the situation

Removal of the patient to a *tropical climate* for example Puerto Rico (Coburn 1931) or southern Florida (our own experience Jones White Roche Perdue and Ryan 1931 to 1936 inclusive reported in 1937) from the north during the colder seasons has been found generally to act favorably in restoring health to children who show an active rheumatic state although beneficial as a rule *it cannot be regarded as specific and it is an expensive*

procedure often not justifiable Permanent residence in the tropics is preferable if a rheumatic family can readily arrange it

During convalescence massage and then the simple exercises of walking lifting and carrying will help to restore normal circulation and muscle function in the extremities Special graded exercises are not necessary if common sense is used Of great help in many cases has been recreational and even occupational therapy during convalescence and during the acute infectious stage membership in the In Bed Club for Children developed by Edith Terry of the Massachusetts General Hospital has greatly aided the morale of many hundreds of youngsters and their families

Tonsillectomy is advisable in many patients with chronic rheumatic heart disease provided their tonsils are infected or abnormally large and provided their hearts are in satisfactory condition to stand the operation as they usually are It is also to be recommended in many cases following active rheumatic infection *after* convalescence is well established It has been advised and carried out even during the acute stage of the infection apparently sometimes with immediate benefit but certainly sometimes with exacerbation of trouble this procedure is not to be recommended in most cases during the active process The prophylactic effect of *routine* tonsil removal in the case of rheumatic infection (rheumatic fever chorea heart disease) has however been disappointing there has been only slight evidence that it protects against either initial or recurrent attacks If the tonsils are however infected or enlarged or if there are repeated attacks of tonsillitis complete tonsillectomy should certainly be done in such cases it is undoubtedly beneficial in the long run The adenoid tissue in the nasopharynx should be removed with the tonsils If the operation is done in very young children it usually has to be repeated after some years because of the new growth of lymphoid tissue in the pharynx

Roentgen irradiation of the heart has also been tried in the therapy of active rheumatic infection (acute endocarditis and myocarditis) but its value has not been confirmed

Surgical treatment of chronic rheumatic heart disease is limited to but very few cases Despite the failure of mitral valvulotomy over 20 years ago renewed attempts are underway at present to apply surgical therapy to valve defects but it is as yet too early to gauge the results or even to prophesy the various technics that will be applied even plastic replacements have been suggested One special condition due to rheumatic heart disease has however already been dramatically helped by surgery and that is recurrent pulmonary edema secondary to tight mitral stenosis Three methods have been used which will be described in more detail in Chapter 26 They consist of (1) production of an atrial septal defect to relieve the high pressure in the left atrium and lungs (2) more practically and effectively to anastomose a right pulmonary vein to the vena azygos major and (3) probably best of all the surgical separation at their commissures of the adherent cusps of the mitral valve

For acute pericardial effusions paracentesis is necessary in rare cases only Chronic pericarditis of rheumatic origin is not the type requiring surgery in contrast to that due to tuberculosis

Prevention The prevention of rheumatic fever and thereby of rheumatic heart disease has become a practical reality It consists to date of several procedures (1) improvement of living conditions (2) protection against hemolytic streptococcus infection by contact with an infected individual (3) the prophylactic use of penicillin in the case of a susceptible person when there is such contact or when such infection begins in the individual concerned and (4) avoidance when possible of residence in climatic areas (high and cold in particular) where hemolytic streptococcus infection and rheumatic fever are common

Differential diagnosis Rheumatic heart disease in active form has to be differentiated from any acute infection especially if there happen to be heart murmurs The differentiation is generally easy in older children and adults because of joint and heart signs and symptoms but in very young children in whom the rheumatic infection is ill defined the problem may be a very difficult one to be solved only by continued and careful observation In young adults with chronic rheumatic heart disease it may sometimes be difficult to distinguish at first whether a new infection is a recurrent rheumatic attack or subacute bacterial (Streptococcus viridans) endocarditis The fewer joint symptoms longer course wider temperature swings greater anemia and eventual appearance of characteristic signs of embolism clubbed fingers splenomegaly and positive blood culture gradually allow the differentiation of subacute bacterial endocarditis from acute rheumatism The intradermal reaction to the toxic filtrate of the hemolytic streptococcus is generally positive in the rheumatic infection and generally negative in subacute bacterial endocarditis this is helpful but not conclusive It is important to note that the active rheumatic infection and subacute bacterial endocarditis may occur simultaneously in the same case (Kelson and White 1945)

Septic chronic or rheumatoid arthritis offers as a rule little difficulty in the differential diagnosis except when there happens to be a complication of heart disease or delayed A V conduction or when both diseases are present in the same case then careful study is needed Rare cases are however insoluble there being no sharp boundary line especially between rheumatoid arthritis and rheumatic fever

Chronic rheumatic heart disease must be differentiated from conditions like severe anemia which give rise to functional cardiac dilatation and murmurs This is generally easily done by the discovery of the underlying cause such as anemia and by the history which shows that the heart symptoms or signs appeared for the first time after the onset of the underlying disease

The rheumatic type of heart disease must be differentiated from other types not always an easy procedure The age the history of rheumatic infection family incidence the preponderant mitral valve involvement and the absence of other causative factors like syphilis thyrotoxicosis hypertension and cor

onary disease usually distinguish primary rheumatic heart disease from other types It is to be remembered however that two or three different factors may simultaneously cause heart disease in a given case much care and good judgment must be exercised not only to determine these causes but also to decide their relative responsibility

BIBLIOGRAPHY

RHEUMATIC HEART DISEASE

Altschule M D "The Relation Between Prolonged P R Interval and Auricular Fibrilla tion in Patients with Rheumatic Heart Disease *Am Heart J* 1939 XVIII 1

Aschoff L Zur Myocarditis Frage" *Verhandl d deutsch path Gesellsch* 1904 VIII 46

Baehr G and Schifrin A "The Rarity of Glomerulo-nephritis in Rheumatic Fever and Its Significance" *Libman Anniversary Volumes* 1932 I 125

Bland, E F, and Jones T D "Clinical Observations on the Events Preceding the Appearance of Rheumatic Fever" *J Clin Investigation* 1935 XIV 633

Bland, E F Jones T D and White P D Disappearance of the Physical Signs of Rheumatic Heart Disease" *J.A.M A* 1936 CVII 569

Bland F F White P D and Jones T D 'The Development of Mitral Stenosis in Young People with a Discussion of the Frequent Misinterpretation of a Middiastolic Murmur at the Cardiac Apex" *Am Heart J* 1935 X, 995

Bouillaud, J *Traite clinique du rhumatisme articulaire* J B Bailliere Paris 1840

Brown M G and Wolff L "Recovery from Acute Rheumatic Fever Without Perma nent Cardiac Damage" *New England J Med* 1940 CCXXIII 242

Bruenn H G The Mechanism of Impaired Auriculoventricular Conduction in Acute Rheumatic Fever *Am Heart J* 1937 XIII 413

Chang, F C and Dieuaide F R "Clinical Study of Rheumatic Fever in China" *Chinese M J* 1937 LI 581

Chavez, I "The Incidence of Heart Disease in Mexico *Am Heart J* 1942 XXIV 88

Clawson B J "Rheumatic Heart Disease" *Am Heart J* 1940 XX 454

Coburn A F *The Factor of Infection in the Rheumatic State* Williams and Wilkins Co Baltimore 1931

"Relationship of the Rheumatic Process to the Development of Alterations in Tissues" *Am J Dis Child* 1933 XLV 933

"Salicylate Therapy in Rheumatic Fever Rational Technic" *Bull Johns Hopkins Hosp* 1943 LXXIII 435

Coburn A F and Moore L V "A Follow up Report on Rheumatic Subjects Treated with Sulfanilamide" *J A.M.A* 1941 CXVII 176

Coombs C F *Rheumatic Heart Disease* with an Introduction by F J Poynton John Wright & Sons Ltd London 1924

Decherd, G M Jr and Herrmann G R Rheumatic Heart Disease in Texas" *Texas State J Med* 1943 XXXIX 229

Fahr T "Beitrag zur Frage der rheumatischen Granulomatose (Polyarthritis rheumatica Rheumatismus infectiosus Graff)" *Klin Wchnschr* 1929 VIII 1995

Faulkner J M and White P D "The Incidence of Rheumatic Fever Chorea and Rheumatic Heart Disease with Especial Reference to Their Occurrence in Families" *J.A.M A* 1924 LXXXIII 425

Ferris E B Jr and Myers W K "Initial Attacks of Rheumatic Fever in Patients Over Sixty Years of Age" *Arch Int Med* 1935 LV 809

Geiger J C Sampson J J Miller R C and Gray J P "A Survey of Heart Disease Morbidity in San Francisco" *Am Heart J* 1936 XII 137

Gelfman R "The Incidence of Acute and Subacute Endocarditis in Rheumatic Heart Disease" *Ann Int Med* 1943 XIX 253

Goldblatt H "Rheumatic Pancarditis with Functional and Anatomical Lesions of All Four Valves" *Libman Anniversary Volumes* 1932 II 507

Graham H C Rheumaticosis *J Oklahoma M A* 1932 XXV 427
Gross L and Fried B M Lesions in Auriculoventricular Conduction System Occuring in Rheumatic Fever *Am J Path* 1936 XII 31
Gross L and Friedberg C K Lesions of Cardiac Valve Rings in Rheumatic Fever *Am J Path* 1936 XII 469
Hansen A E Platou R V and Dwan P F Prolonged Use of Sulfonamide Compound in Prevention of Rheumatic Recrudescences in Children Evaluation Based on Four Year Study on Sixty four Children *Am J Dis Child* 1942 LXIV 963
Harrison T R and Levine S A Notes on the Regional Distribution of Rheumatic Fever and Rheumatic Heart Disease in the United States *South M J* 19 4 XVII, 914
Hedley O F Trends Geographical and Racial Distribution of Mortality from Heart Disease Among Persons 5-24 Years of Age in the United States During Recent Years (1922-1936) *U S Pub Health Rep* 1939 LIV 2271
Hochrein M Uber Angina Pectoris bei Mitralstenose *Deutsch Arch f klin med* 1930 CLXIX 195
Howard C P The Rheumatic Lung *Ann Int Med* 1933 VII 165
Hubbard J P and Griffin W A Open Air Sanatorium Care for Patients with Rheumatic Fever and Rheumatic Heart Disease *New England J Med* 1940 CCXXIII 968
Jones T D and Bland E F Clinical Significance of Chorea as a Manifestation of Rheumatic Fever A Study in Prognosis *J A M A* 1935 CV 571
Rheumatic Fever and Heart Disease Completed Ten Year Observations on 1000 Patients *Tr A Am Physicians* 1942 LVII 267
Jones T D White P D Roche C F Perdue J J and Ryan H A "The Transportation of Rheumatic Fever Patients to a Subtropical Climate *J A M A* 1937 CVIII 1308
Kaiser A D Results of Tonsillectomy A Comparative Study of Twenty two Hundred Tonsillectomized Children with an Equal Number of Controls Three and Ten Years after Operation *J A M A* 1930 XCV 837
Kissane R W and Koons R A Intra Uterine Rheumatic Heart Disease" *Arch Int Med* 1933 LII 905
Kuttner A G and Reyersbach G The Prevention of Streptococcal Upper Respiratory Infections and Rheumatic Recurrences in Rheumatic Children by the Prophylactic Use of Sulfanilamide *J Clin Investigation* 1943 XXII 77
Medical Research Council England "Social Conditions and Acute Rheumatism Special Report Series No 114 *Report of Committee on Child Life Investigations* London 1927
Mote J R and Jones T D Studies of Hemolytic Streptococcal Antibodies in Control Groups Rheumatic Fever and Rheumatoid Arthritis *J Immunol* 1941 XLI 35
Paul J R "Pleural and Pulmonary Lesions in Rheumatic Fever *Medicine* 19 8 VII 383
The Epidemiology of Rheumatic Fever and Some of Its Public Health Aspects American Heart Association New York 2nd ed 1943
Paul J R and Dixon G L Climate and Rheumatic Heart Disease A Survey Among American Indian School Children in Northern and Southern Localities" *J A M A* 1937 CVIII 2096
Perry C B "Rheumatic Heart Disease in Identical Twins *Arch Dis Childhood* London 1940 XV 177
Poynton F J and Paine A *Researches on Rheumatism* J and A Churchill London 1913
Rabinowitz M A Rheumatic Pneumonia *J A M A* 1926 LXXXVII 142
Reyersbach C and Kuttner A G "Studies on the Auriculoventricular Conduction Time of Normal Children and of Rheumatic Children Without Signs of Rheumatic Activity" *Am Heart J* 1940 XX 573
Robey W H (Representing New England Heart Association) "A Cardiac Survey of Children in Boston Public Schools" *Nation s Health* 1927 IX No 12 p 21
Schwarz, H "An Unusual Case of Acute Rheumatic Fever in an Infant" *Libman Anniversary Volumes* 1932 III 1061

Seegal D and Seegal B C Studies in the Epidemiology of Rheumatic Fever Annual Incidence in Some Hospitals in the United States Its Possessions and Canada" *J A M A* 1927 LXXXIX 11

St Lawrence W The Family Association of Cardiac Disease Acute Rheumatic Fever and Chorea A Study of One Hundred Families" *J A M A* 1922 LXXIX 2051

Stone C T and Vanzant F R Heart Disease as Seen in a Southern Clinic A Clinical and Pathological Survey *J A M A* 1927 LXXXIX 1473

Swift, H F Rheumatic Heart Disease Pathogenesis and Etiology in Their Relation to Therapy and Prophylaxis *Medicine* 1940 XIX 417

Features Which Suggest Public Health Consideration of Rheumatic Fever *Bull New York Acad Med* 1940 XVI 501

Thomas C B and France R (and Reichsman F) Prophylactic Use of Sulfanilamide in Patients Susceptible to Rheumatic Fever" *Bull Johns Hopkins Hosp* 1939 LXIV 67 (and *J A M A* 1941 CXVI 551 and *Bull New York Acad Med* 1942 XVIII 508)

von Glahn W C "Auricular Endocarditis of Rheumatic Origin *Am J Path* 1926 II 1

Walsh B J and Sprague H B Character of Congestive Failure in Children with Active Rheumatic Fever *Am J Dis Child* 1941 LXI 1003

Wedd A M Complete Heart Block in Acute Rheumatic Fever *Am Heart J* 1937 XIV 759

Wells W C On Rheumatism of the Heart *Tr Soc Improvement M and Chir Knowledge* London 1810 CXI 372

White P D Acute Heart Block Occurring as the First Sign of Rheumatic Fever *Am J M Sc* 1916 CLII 589

White P D and Bland E F Mitral Stenosis After Eighty *J A M A* 1941 CXVI 2001

White P D and Jones T D Heart Disease and Disorders in New England *Am Heart J* 1928 III 302

Wilson M G *Rheumatic Fever* The Commonwealth Fund New York 1940

Wood J E Jr Jones T D and Kimbrough R D The Etiology of Heart Disease Clinical Study of 623 Cases with Certain Observations on Race and Climate *Am J M Sc* 1926 CLXXII 185

Recent References (1944–1950)

Appleman D H Feiman M S and Harris L Acute Rheumatic Fever in the Aged" *Am Heart J* 1949 XXXVII 982

Armstrong D B and Wheatley G M Studies in Rheumatic Fever Metropolitan Life Ins Co New York 1944

Ash R Rheumatic Infection in Childhood Fifteen to Twenty Year Follow up Caution Against Early Ambulant Therapy *Am J Dis Child* 1948 LXXVI 46

Barber H S Rheumatic Fever in R A F Results of Treatment at Convalescent Center *Brit M J* 1946 II 83

Barnes A R Effects of Cortisone and ACTH in 14 Patients with Acute Rheumatic Fever" *Proc Staff Meet Mayo Clinic* 1950 XXV 478

Barroso-Moguel R and Costero I Evolución de las lesiones valvulares durante la fiebre reumática" *Arch del Inst de cardiol de Mexico* 1949 XIX 663

Blackman N S and Hamilton C I Jr Serial Electrocardiographic Changes in Young Adults with Acute Rheumatic Fever Report of 62 Cases" *Ann Int Med* 1948 XXIX 416

Blanchard K C et al The Effect of 3 Hydroxy 2 Phenylcinchoninic Acid upon Rheumatic Fever" *Bull Johns Hopkins Hosp* 1950 LXXXVII 50

Bos A K Some Observations on the Past History and Clinical Studies in Rheumatic Heart Disease as Found in Bengal *Indian Heart J* 1949 I 68

Cannon J F Incidence of Rheumatic Heart Disease in Rocky Mountain Region" *Rocky Mountain M J* 1946 XLIII 25

Coburn A F and Young D C *The Epidemiology of Hemolytic Streptococcus* Williams & Wilkins Co Baltimore 1949

Cortes C and Villarreal H "Revision de 1 160 Casos de Endocarditis Valvular Reu

matica Aspectos clinicos" *Arch del Inst de Cardiol de Mexico* 1947 XVII 775 and *Am Heart J* 1947 XXXIII 715
Craige E Alimurung M M Bland E F and Massell B F 'The Q T Interval in Rheumatic Fever *Circulation* 1950 I 1338
Crowley N "Hyaluronidase Production by Hemolytic Streptococci of Human Origin *J Path & Bact* 1944 LVI 27
Denny F W Wannamaker L W Brink W R Rammelkamp C H Jr and Custer E A Prevention of Rheumatic Fever Treatment of the Preceding Streptococcic Infection *J A M A* 1950 CXLIII 151
Dodge K G Baldwin J S and Weber M W Prophylactic Use of Sulfanilamide in Children with Inactive Rheumatic Fever *J Pediat* 1944 XXIV 483
Edstrom G "Can Rheumatic Infection Be Influenced by Artificial Tropical Climate" *Acta med Scandinav* 1944 CXVII 376
Erganian J A Forbes G B and Case D M Salicylate Intoxication in Infant and Young Child Report of 13 Cases *J Pediat* 1947 XXX 129
Fashena G J "The Incidence of Rheumatic Fever in Texas with Particular Reference to the Dallas Area *Texas State J Med* 1944 XXXIX 474
Feasby W R Rheumatic Fever in the Canadian Army *War Med* 1944 VI 139
Filberbaum M B Griffith G C Solley R F and Leake W H Electrocardiographic Abnormalities in 6 000 Cases of Rheumatic Fever *California & West Med* 1946 LXIV 340
Fischel E E and Pauli R H "Serologic Studies in Rheumatic Fever I Phase' Reaction and Detection of Autoantibodies in the Rheumatic State *J Exper Med* 1949 LXXXIX 669
Foster F P McEachern G C Miller J H Ball F E Higley C S and Warren H A 'The Treatment of Acute Rheumatic Fever with Penicillin" *J A M A* 1944 CXXVI 281
Francisco R Rheumatic Heart Disease in the Tropics with Special Reference to Its Incidence in Puerto Rico" *J B Lippincott Co Clinics* 1947, V 971
Freud P Rook G D and Brunhofer A Reactivation of Rheumatic Fever by Smallpox Vaccination *J Pediat* 1950 XXXVI 635
Gardner F E and White P D "Coronary Occlusion and Myocardial Infarction Associated with Chronic Rheumatic Heart Disease" *Ann Int Med* 1949 XXXI 1003
Glendy R E Rheumatic Diseases in Southwestern Virginia *Virginia M Monthly* 1948 LXXV 334
Goerner J R Massell B F and Jones T D Use of Penicillin in the Treatment of Carriers of Beta Hemolytic Streptococci Among Patients with Rheumatic Fever *New England J Med* 1947 CCXXXVII 576
Griffith G C Moore F J McGinn S and Cosby R S Familial Incidence of Rheumatic Fever II A Statistical Study of the Familial and Personal History of Rheumatic Fever *Am Heart J* 1948 XXXV 444
Hardgrove M Whittier L and Smith E R. "Rheumatic Fever in Panama" *J A M A* 1946 CXXX 488
Harris T N "Failure of Massive Salicylate Therapy to Suppress the Inflammatory Reaction in Rheumatic Fever" *Am J M Sc* 1947 CCXIII 482
"Studies on the Relation of the Hemolytic Streptococcus to Rheumatic Fever I Review of Serologic Literature" *Am J Dis Child* 1948 LXXVI 411
Harris T N Abrams W B Leo T F P and Hubbard J P "Cortisone Therapy in Acute Rheumatic Carditis Preliminary Observations" *Circulation* 1951 III 215
Harris T N and Harris S "Studies in the Relation of the Hemolytic Streptococcus to Rheumatic Fever V Streptococcal and Anti hyaluronidase (mucin-clot prevention) Titers in the Sera of Patients with Rheumatic Fever Streptococcal Infection and Others" *Am J M Sc* 1949 CCXVII 174
Hartz, P H and Van der Sar A "Occurrence of Rheumatic Carditis in Native Population of Curaçao Netherlands West Indies" *Arch Path* 1946 XLI 32
Hench, P S Kendall E C Slocumb C H and Polley H F "Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis Rheumatic Fever and Certain Other Conditions A Study in Clinical Physiology" *Arch Int Med* 1950 LXXXV 545
Hench P S Slocumb C H Barnes A R Smith H L Polley H F and Kendall,

E C "The Effects of the Adrenal Cortical Hormone 17 hydroxy 11-dehydrocorticosterone (Compound E) on the Acute Phase of Rheumatic Fever Preliminary Report *Proc Staff Meet Mayo Clinic* 1949 XXIV 277
Holoubek J E, and Holoubek A B Heart Disease in the South II A Statistical Survey of One Hundred Seventeen Deaths Due to Rheumatic Heart Disease *Am Heart J* 1947 XXXIV 709
Jones, T D "The Diagnosis of Rheumatic Fever *J A M A* 1944 CXXVI 481
Jucà, A and White P D "The Cause of Death in Rheumatic Heart Disease in Adults" *J A M A* 1944 CXXV 767
Keith, J D, and Pequegnat L A "Some Observations on the Prevalence of Rheumatic Heart Disease in Canada" *Canad J Pub Health* 1947 XXXVIII 111
Kelson, S R and White P D "Notes on 250 Cases of Subacute Bacterial (Streptococcal) Endocarditis Studied and Treated Between 1927 and 1939 *Ann Int Med* 1945 XXII 40
Kohn K H Milzer A and MacLean H Oral Penicillin Prophylaxis of Recurrences of Rheumatic Fever Interim Report on Method After a Three Year Study *J A M A* 1950 CXLII 20
Kuttner A G "Sulfonamide Prophylaxis for Prevention of Rheumatic Recurrences" *J Pediat* 1945 XXVI 216
Levine H D "Rheumatic Heart Disease in New Guinea Including Cardiovascular Survey of 200 Native Papuans" *Ann Int Med* 1946 XXIV 826
Logue R R and Hurst J W "Suspected Age of Onset of Twenty-six Patients with Rheumatic Fever Who Are Five Years of Age or Under In press 1951
Lustok M J and Kuzma J F "Rheumatic Pneumonitis A Clinical Study of 12 Necropsy Proved Cases of Rheumatic Pneumonitis *J Lab & Clin Med* 1950 XXXVI 958
MacIlwaine Y "The Relationship Between Rheumatic Carditis and Subacute Bacterial Endocarditis" *J Path & Bact* 1947 LIX 557
McKeown E F "Experimental Serum Carditis and Its Relationship to Rheumatic Fever *J Path & Bact* 1947 LIX 547
McMillan R L and Jones C C "Rheumatic Heart Disease in Northwest North Carolina *North Carolina M J* 1950 II 105
Malsner M M and Amsterdam S D Oral Penicillin in Prophylaxis of Recurrent Rheumatic Fever" *J Pediat* 1947 XXXI 658
Masini V "Studio clinico statistico sulla evoluzione e prognosi della cardiopatia reumatica I Evoluzione in general e complicazioni" *Cuore e circola* 1949 XXXIII 26
Studio clinico-statistico sulla evoluzione e prognosi della cardiopatia reumatica III I vizi cardiaci di origine reumatica nei soggetti di età superiore a 45 anni *Cuore e circola* 1949 XXXIII 76
Massell B F *Rheumatic Fever and Rheumatic Heart Disease* Year Book Publishers Chicago 1951 in press
Massell B F Dow J W and Jones T D "Orally Administered Penicillin in Patients with Rheumatic Fever" *J A M A* 1948 CXXXVIII 1030
Massell B F and Warren J E Effect of Pituitary Adrenocorticotropic Hormone (ACTH) on Rheumatic Fever and Rheumatic Carditis" *J A M A* 1950 CXLIV 1335
Massell B J Warren J E Patterson P R and Lehmus H J Antirheumatic Activity of Ascorbic Acid in Large Doses Preliminary Observations on Seven Patients with Rheumatic Fever *New England J Med* 1950 CCXLII 614
Massell B F Warren J E Sturgis G P Hall B and Craige E "The Clinical Response of Rheumatic Fever and Acute Carditis to ACTH *New England J Med* 1950 CCXLII 641 and 692
Meyer K "The Biological Significance of Hyaluronic Acid and Hyaluronidase" *Physiol R v* 1947 XXVII 335
Milzer A, Kohn K H and MacLean H "Oral Prophylaxis of Rheumatic Fever with Penicillin Resistant Hemolytic Streptococci" *J A M A* 1948 CXXXVI 536
Murphy G E and Swift, H F "Induction of Cardiac Lesions Closely Resembling Those of Rheumatic Fever in Rabbits Following Repeated Skin Infections with Group A Streptococci *J Exper Med* 1949 LXXXIX 687
The Induction of Rheumatic like Cardiac Lesions in Rabbits by Repeated Focal

Infections with Group A Streptococcus Comparison with the Cardiac Lesions of Serum Disease" J Exper Med 1950 XCI 485

Neuberger K T Geever E F and Rutledge E K "Rheumatic Pneumonia" *Arch Path* 1944 XXXVII 1

Perez de los Reyes R de la Torre H Labourdette Scull J M and Junco J A La cardiopatia reumatica en el nino cubano" *Arch de med Infantil* 1944 XIII 3

Pitt Evans J A Discussion on the Management of Rheumatic Fever and Its Early Complications Oral Penicillin in the Prophylaxis of Streptococcal Infection and Rheumatic Relapse" *Proc Roy Soc Med* 1950 XLIII 206

Quinn R W Rheumatic Heart Disease and Crowding A Survey of Rural and Urban Connecticut School Children *Am J Pub Health* 1948 XXXVIII 1071

Reid J Watson R D and Sproull D H "Mode of Action of Salicylate in Acute Rheumatic Fever" *Quart J Med* 1950 XIX 1

Rich A R and Gregory J E "Further Experimental Cardiac Lesions of Rheumatic Type Produced by Anaphylactic Hypersensitivity *Bull Johns Hopkins Hosp* 1944 LXXV 115

Robles Gil J "Incidence and Clinical Features of Rheumatic Fever in Mexico City *Am Heart J* 1947 XXXIII 713

Rothbard S Group A Streptococcal Infections and Rheumatic Fever" *Michigan S M Soc J* 1949 XLVIII 1126

Rutstein D D "Need for a Public Health Program in Rheumatic Fever and Rheumatic Heart Disease" *Am J Pub Health* 1946 XXXVI 461

Sampson J J Hahman P T Halverson W L and Shearer M C "Incidence of Heart Disease and Rheumatic Fever in School Children in Three Climatically Different California Communities" *Am Heart J* 1945 XXIX 178

Sprague H B and Carmichael D B Jr "Rheumatic Valvular Disease in the Aged *Geriatrics* 1950 V 239

Svartz N and Ernberg T The Prognosis in Different Kinds of Rheumatic Valvular Lesions" *Nord med* 1947 XXXIII 757

Wedum B G Darley W and Rhodes P H Prevalence of Rheumatic Heart Disease at High Altitudes" *Am J Dis Child* 1950 LXXIX 205

Wegria R and Smull K "Salicylate Therapy in Acute Rheumatic Fever" *J Pedi* 1945 XXVI 211

Wheatley G M "Rheumatic Fever A Summary of Present Concepts" *Pediatrics* 1949 III 680

White P D "The Relative Incidence of the Etiologic Types of Heart Disease in New England Compared to That of 25 Years Ago An Analysis of 3000 Cases" 1951 *in press*

Wilson M G and Helper H N "Effect of Pituitary Adrenocorticotropic Hormone (ACTH) in Acute Rheumatic Carditis *J A M A* 1951 CXLV 133

Wilson M G and Lubschez, R "Longevity in Rheumatic Fever Based on Experiences in 1 042 Children Observed Over a Period of Thirty Years." *J A M A* 1948 CXXXVIII 794

Young W R and Viko L E "Rheumatic Fever in School Children in Utah *Rocky Mountain M J* 1950 XLVII 426

CHAPTER 15

ACUTE AND SUBACUTE BACTERIAL (INFECTIVE) ENDOCARDITIS

Penicillin and other new specific therapeutic agents have already greatly reduced the seriousness of the diseases discussed in the present chapter and we may hope that eventually the reduction or even complete control of hemolytic streptococcus and other infections and of rheumatic and congenital heart disease may render it obsolete Much of what was printed in earlier editions of this book is now merely of historical interest

A discussion of acute and subacute bacterial (infective) endocarditis (malignant endocarditis) follows naturally after the last two chapters because bacterial endocarditis has been frequent in early adult life and has been in its subacute form an important complication of rheumatic and of congenital heart disease

These two types of cardiac infection have been called acute bacterial endocarditis and subacute bacterial endocarditis respectively because of their clinical characteristics This terminology is useful for general discussion and classification but not so satisfactory as is the terminology based on the specific causative bacteria the names of which should always be employed in preference to the general term provided we know what the bacteria are For example Staphylococcus aureus or pneumococcus endocarditis is preferable to acute bacterial endocarditis as a diagnosis and Streptococcus viridans or alpha hemolyticus endocarditis is a better term than subacute bacterial endocarditis The word infective is sometimes employed instead of bacterial and in former days both of these groups of infection of the heart were classed together as malignant endocarditis a designation with much justification because of the almost invariably fatal outcome in those days but unsuitable because of the customary restriction of the word malignant to new growths and because of the high recovery rate nowadays

In a large series of cases of acute and subacute bacterial endocarditis (199 cases with 138 autopsies) studied 25 years ago the responsible organisms were found as shown in Table 7 page 386

Acute and subacute bacterial endocarditis are alike in that they are b serious diseases attended by invasion of the endocardium by virulent org isms almost wholly of the coccus family, there may be a similar invasion the walls of the great arteries (bacterial endarteritis) The duration and vi lence of the diseases are the only points in which they differ clinically A arbitrary borderline of two months has been set between them If the infect is a violent one lasting but a few days or weeks it has been called acute ba terial endocarditis if it is slow in its course lasting over two or three mont

Table 7

BACTERIA CAUSING INFECTIVE BACTERIAL ENDOCARDITIS

	Per Cent
Streptococcus	57
Pneumococcus	14
Staphylococcus aureus	13
Gonococcus	11
Influenza bacillus	4
Staphylococcus albus	1 (Thayer 1925)

it has been called subacute bacterial endocarditis Generally the latter is cause by one organism the Streptococcus viridans while the former is caused by any one of a large number of organisms Rarely a Streptococcus viridans in fection is so rapid that it falls into the acute bacterial group and rarely one of the other organisms is so much resisted that it falls into the subacute bacterial group as happens infrequently in the case of the gonococcus or of the influenza bacillus

A high mortality was once characteristic of these diseases, prior to the use of penicillin early in 1944 but now recoveries are the rule and preventive measures are also highly effective especially in the case of the acute type Mild infection with these organisms resulting in demonstrable valvular deformity after recovery may possibly account for some of the chronic valvular disease found in cases without a history of a rheumatic infection but the extent to which this occurs is not actually known and must be regarded still as an open question In the present state of our knowledge it is reasonable to assume that the majority of cases of chronic nonsyphilitic valvular disease are rheumatic in origin

Finally there is a considerable number of cases of very fresh endocarditis of slight or moderate degree discovered only by the pathologist at postmortem examination of individuals dying of a great variety of diseases Such terminal endocarditis is of academic and pathologic interest alone for it usually cannot be diagnosed clinically and has little or nothing to do with the death of the patient We do not ordinarily designate under the term acute bacterial endocarditis this slight terminal endocarditis that has little or no clinical significance

ACUTE BACTERIAL ENDOCARDITIS

Acute bacterial endocarditis or endarteritis consists of an acute nonrheumatic invasion of endocardium or arterial endothelium either uncomplicated or as a part of other acute illness it is attended by the symptoms and signs of a severe infection and in days gone by ended often in fact usually in death in the course of two months but now recovery is the rule in the rare cases that still appear Cases in which it occurs number well under 1 per cent of all types of heart disease and of all types of endocarditis if we exclude the terminal endocarditis that has no clinical significance

Etiology *Cause* The bacterium responsible for this disease may be any one of several organisms generally either the Streptococcus hemolyticus the Staphylococcus aureus the Bacillus coli communis the pneumonococcus the gonococcus or the meningococcus These six infecting organisms had been found in acute bacterial endocarditis in Boston before the days of penicillin in the following relative frequency making up nearly 100 per cent of the total of cases the Streptococcus hemolyticus 43 6 per cent the Staphylococcus aureus 22 8 per cent the Bacillus coli communis 10 5 per cent the pneumococcus 8 4 per cent the gonococcus 4 2 per cent and the meningococcus 4 2 per cent (Phipps 1932 with additional data by Dexter personal communication a total of 48 autopsied cases of acute bacterial endocarditis)

Other bacteria that have been reported as rare causes of acute bacterial endocarditis are the Staphylococcus albus the typhoid bacillus the enterococcus the Micrococcus tetragenus the Bacterium acidi lactici the Streptococcus viridans the parainfluenza bacillus (Russell and Fildes 1928 Fox 1935) the plague bacillus Brucella melitensis (Malta or undulant fever bacterium) and the Micrococcus endocarditidis rugatus

These organisms enter the circulation and attack the heart usually in the course of severe illness elsewhere in the body such as pneumonia puerperal infection gonorrheal rheumatism abscesses pyemia tonsillitis and meningitis In one series of 400 fatal cases of pneumonia examined post mortem 22 instances of pneumococcus vegetative endocarditis were found (Menetrier 1919) and in another series of 337 fatal cases of pneumonia there were 14 cases of pneumococcus endocarditis (4 15 per cent) (Lord 1932) In a series of 402 fatal cases of puerperal fever acute streptococcus endocarditis was found 8 times (Ruiz and Garcia 1926) Happily all this is now essentially past history since there is at present specific therapy for almost all these primary infections

There is another source of infection that is not yet under adequate control and that is septicemia (especially with a staphylococcus) resulting from the self medication hypodermically by narcotic addicts (Hussey et al 1944 Luttgens 1949) In such cases there is usually no pre-existing valvular disease

Age Acute bacterial endocarditis may occur at any age from infancy to

old age but it is most frequent in the fifth decade It may rarely occur also in fetal life

Sex Males are more subject to the disease than are females (73 per cent males to 27 per cent females in Phipps series 1932)

Predisposing factors Although this acute cardiac infection may occur in hearts previously undamaged it is more likely to attack those hearts already diseased with rheumatic lesions or congenital defects or arteriosclerotic changes where the soil is more suitable (60 per cent of Phipps series 1932)

Pathology In acute bacterial endocarditis the valve cusps and frequently also the chordae tendineae and endocardium of atrium or ventricle (more commonly the left) and sometimes even the intima of aorta or patent ductus arteriosus are the site of the deposition of thrombi called vegetations these vegetations are of varying size sometimes as large as peas or beans and they consist of irregular masses of fibrin leukocytes and colonies of bacteria Any valve may be markedly involved but the pulmonary is only rarely affected In acute bacterial endocarditis though less strikingly than in rheumatic heart disease the valves of the left side of the heart are more frequently involved than those of the right side The aortic valve is about as frequently affected as is the mitral In a series of 23 cases of pneumococcus endocarditis the left side of the heart was involved alone in 18 the right side alone in 3 and both sides in 2 while the mitral valve was affected in 13 the aortic valve in 12, both mitral and aortic valves in 5 and the tricuspid in 5 in one of which the pulmonary valve also was involved (Lord 1932) in a series of 58 cases of gonococcus endocarditis the valve lesions were left sided in 48 and the aortic valve was involved in 35 of these (Lion and Levy Bruhl 1922)

Ulceration of the endocardium of valve or heart wall or of the wall of the aorta or other arteries is common in the more severe cases this is sometimes followed by perforation or aneurysms of cusps rupture of chordae tendineae abscesses of the valve rings and even by small aneurysmal cavities in the aortic or other arterial wall (called mycotic aneurysms)

With recovery scarring undoubtedly takes place but whether or not such recovery is responsible for a few of the cases of chronic aortic or mitral stenosis we have no certain knowledge

Coincident myocardial or pericardial disease is uncommon There may be found pyemic abscesses in the heart muscle or infarction due to coronary embolism arising from thrombi on the endocardium septic pericarditis is also possible in such cases but is rare

Symptoms The symptoms of acute bacterial endocarditis are simply those of any very severe infection with septicemia fever of septic type with wide swings as a rule often with normal temperature in the morning and 103, 104° (40° C) or 105 F in the evening chills and sweating prostration and delirium In addition, if the disease continues as long as a few weeks there tend to be symptoms from embolism caused by pieces of the endocardial thrombi blocking arteries to viscera extremities or brain and pain and other localizing symptoms such as hemoptysis from pulmonary infarction or hemiplegia from

cerebral embolism The involvement of the heart itself rarely causes symptoms

Signs The patient appears very sick with little to point to the source of trouble except for embolic phenomena and the appearance of anemia and heart murmurs (or their increase) if the disease lasts long enough Sometimes there are no definite signs the fever being accounted for by other evidence of infection while the heart condition is discovered only at postmortem examination There is usually a high (polymorphonuclear) leukocytosis of 20 000 to 30 000 or more unless the infection has completely overwhelmed the resistance of the patient A secondary anemia develops rapidly but does not become so severe as in the subacute variety of bacterial endocarditis because of the short duration of the disease There may be petechial hemorrhages into the skin and in rare cases even extensive purpura There may be defective atrioventricular conduction shown by increase of the *P R* interval of the electrocardiogram beyond 0 2 second but this is rare Arrhythmias are very uncommon The most important method of study is that of blood culture In the presence of this disease a positive blood culture is usually obtained at the second or third attempt if not at the first the cause of the infection is thus discovered

Course and prognosis Acute bacterial endocarditis formerly progressed in rapid strides to a fatal termination in the course of days or weeks Death was usually the result of toxemia but sometimes it came from embolism of brain lung or coronary circulation Very infrequently was it due to heart failure The beginning of effective specific therapy by penicillin the sulfonamides and other medication during the past decade has changed the picture completely so that now fatalities are uncommon and acute bacterial endocarditis is usually cured before it starts by the control of the underlying disease whether pneumonia meningitis gonorrhea or other acute infection Thus the diagnosis of acute bacterial endocarditis has now become not only very difficult but also very rare It can still be suspected by the careful physician who notes the onset of the heart murmurs of valvular involvement during the course of pneumonia or sepsis and who observes the persistence of these murmurs and the development of cardiac enlargement on recovery

Complications Embolism secondary anemia and heart failure have already been noted as important complications Another occasional complication that may be serious or even fatal is the tendency to hemorrhages such as may occur in any fulminating infection—purpura of skin sclerae and mucous membranes and bleeding from nose mouth lungs or gastrointestinal tract

Treatment In the second edition of this book fourteen years ago it was stated that there is no specific treatment for the disease except in the very rare case of meningococcus endocarditis when the administration intravenously of active antimeningococcus serum may effect a cure that when the pneumococcus of type 1 or type 2 is responsible it would seem rational to inject antipneumococcus serum that in most cases of acute bacterial endocarditis all kinds of drugs vaccines and serums have been tried in vain that

transfusions also have failed and that the rare recovery except ' antimeningococcus serum may help is due apparently to the patient s resistance which is to be supported by every measure at one s comm chiefly by good nursing care, food, quiet and avoidance of the administr of drugs except to relieve discomfort ' A great advance was noted in the ' edition seven years ago consisting of the use of the sulfonamide d (sulfanilimide sulfapyridine, sulfathiazole, and sulfadiazine) which by trolling the underlying infections from pneumococcus, gonococcus stre coccus and staphylococcus prevented, in some cases at least this ser in fact previously fatal complication of acute bacterial endocarditis and today we can happily record another, perhaps final spectacular advance ! penicillin has appeared to help to wipe out this dread disease

Differential diagnosis The two chief difficulties in diagnosis come (1) f easy confusion with the subacute variety of bacterial endocarditis and from confusion with severe infection of other nature especially with sistence or recurrence of the original disease from which the endocar comes In the former case the virulence of the acute variety of bacterial en carditis its shorter course the recent history of other illness and blood cul findings generally make differentiation clear In the latter case the differe tion may be impossible only the development of embolic phenomena of se anemia or of murmurs pathognomonic of valvular involvement (usuall aortic diastolic murmur) may point eventually to acute bacterial endocard It is impossible to distinguish the rare case of recovery with chronic valv disease from one of rheumatic origin unless the pulmonary valve has b affected or the case has been observed during its development in the co of some serious infection like pneumonia

SUBACUTE BACTERIAL ENDOCARDITIS (ALSO CALLED SUBACU INFECTIVE ENDOCARDITIS CHRONIC ULCERATIVE ENDOCARDITIS AND ENDOCARDITIS LENTA)

Subacute bacterial endocarditis as a clinical entity is much more comm than is the acute variety of malignant endocarditis It consists of the invas of the heart—chiefly of the valves—by the Streptococcus viridans rarely the gonococcus or influenza bacillus until recently it resulted fatally afte lingering illness Its frequency and seriousness make it of great importar In New England 20 years ago it occurred in 1 to 2 per cent of all card patients (White and Jones 1928) in 7 to 8 per cent of persons with co genital cardiovascular defects (Abbott) and in about 5 per cent of cases rheumatic heart disease Because of its seriousness subacute bacterial en carditis has a relatively high hospital incidence in comparison with rheum fever for example in the years 1928 to 1931 there were 177 cases of su acute bacterial endocarditis admitted to the larger Boston hospitals in co trast to 772 cases of rheumatic fever (Morrison 1932) The advent of ' sulfonamide derivatives ten years ago altered the situation for the outlo

was no longer entirely hopeless as it had been a moderate number of cures were recorded but the disease was still nearly 95 per cent fatal It was early in 1944 that with proof of the efficacy of penicillin (Loewe) the outlook suddenly brightened and now recovery is possible in at least 80 per cent of the cases Despite this great change in fact because of it a clear recognition of the details of the disease has become all the more important since the earlier the diagnosis is made the sooner the curative treatment can be started and the less will be the added damage to the heart and the risk from the common and serious complications such as embolism

Etiology Cause The organism responsible for subacute bacterial endocarditis is in 90 to 95 per cent of the cases the Streptococcus viridans (Schottmuller 1910) and in the other 5 to 10 per cent the gonococcus influenza or parainfluenza bacillus enterococcus or Brucella abortus The typhoid bacillus has also been reported to give rise to a long-drawn-out endocarditis There may be a mixed infection as by gonococcus and streptococcus (Orgain and Poston 1942 Olinger 1948) or there may be more than one strain of viridans streptococci in the same case (MacLean and Howell 1947) All these other organisms especially the gonococcus can cause a short virulent acute bacterial endocarditis but the Streptococcus viridans rarely does so

Predisposing factors The chief predisposing factor is chronic heart disease particularly old rheumatic valvular disease (in about 80 per cent of the cases) and congenital cardiovascular defects (in about 10 per cent of the cases) especially in those with either bicuspid aortic valves (9 of 32 cases of Abbott s series and 11 of 52 of Gelfman and Levine s series) or ventricular septal defects (13 of 50 cases and 13 of 31 cases respectively) or patency of the ductus arteriosus (21 of 92 cases and 4 of 14 cases) or coarctation of the aorta (7 of 70 cases and one of 10 cases) in contrast to atrial septal defects (2 of 68 cases and none of 45 cases respectively Abbott and Gelfman and Levine 1942) but a previously undamaged heart may infrequently also be the site of this disease Rarely aortic valves damaged by syphilis may be involved in subacute bacterial endocarditis but in such cases there may be a coincident rheumatic valve lesion

Focal infection as in diseased teeth tonsils and gums can be a predisposing factor (Weiss 1934) dental extractions are more commonly followed by subacute bacterial endocarditis than are any other recognizable events There is a clear reason for this as indicated by the findings of Okell and Elliott (1935) in 40 instances after multiple tooth extractions in the presence of extensive disease of the gums positive blood cultures were obtained in 30 (75 per cent) in 60 instances after multiple tooth extractions in the presence of a moderate degree of gum disease there were positive blood cultures in 42 (70 per cent) and in 38 instances of the extraction of one or more teeth without detectable gum disease there were 12 positive blood cultures (34 per cent) The more often one inquires specifically about dental work or infection prior to the onset of subacute bacterial endocarditis the more often one finds it (up to about one third of the cases)

The mechanism of the endocardial involvement in subacute bacterial endocarditis has been variously considered Direct blood stream infection of the endocardium damaged of old with small thrombi or ulcerations as footholds for the streptococci that happen to be circulating in the blood is probably the usual mode of involvement rather than the introduction of these organisms to the endocardium through blood vessels in the valves but it is possible that both methods of infection exist Although the Streptococcus viridans is an occasional invader of the blood stream even in normal persons it causes no disease unless it enters in large numbers (as through foci of infection) or unless conditions favor its lodgment and growth as in individuals with chronic heart disease

Age The age at which subacute bacterial endocarditis occurs varies from early childhood to old age it is commonest between the ages of fifteen and thirty years Of 250 cases in Kelson and White's series (1945) 6 were under ten years 42 between ten and twenty 79 between twenty and thirty 53 between thirty and forty 39 between forty and fifty 21 between fifty and sixty and 10 over sixty The youngest cases on record are one and one half years old (Goetsch 1938) two and one half (complicating congenital heart disease) and five years old but the disease is very rare in young children The oldest cases were eighty two years of age a man who had apparently sclerotic valvular changes as a background of his infection (Willius 1940) and eighty seven years (Zeman 1945) Streptococcus viridans bacteriemia without endocarditis has been reported in two infants shortly after birth the mothers being ill with subacute bacterial endocarditis themselves (Walser 1928) A collection from the literature has been made (Rost and Fischer 1928) of 64 cases under the age of fourteen years

Sex Subacute bacterial endocarditis occurs somewhat more often in males than in females in Kelson and White's series (1945) it was found in 161 males and 89 females and in a series of 328 cases collected by Blumer from the literature the ratio was 60 per cent males to 40 per cent females (Blumer 1923)

Other factors Other factors such as race climate and social and economic status are relatively unimportant compared to that of the presence of chronic heart disease mentioned above except as they favor the predisposing cause namely rheumatic involvement However it is possible though not yet proved that any illness accident or exposure to cold and wet or to strain may help to precipitate the disease by favoring the bacterial invasion

Pathology The pathologic picture in subacute bacterial endocarditis is primarily that of involvement of the endocardium of valves by the deposition of irregular masses of fibrin leukocytes erythrocytes and platelets enclosing bacteria and products of bacterial degeneration, called vegetations (Figures 87 and 88 see opposite page) These vegetations are larger than the thrombi in rheumatic endocarditis but they may not be so large as those of acute bacterial endocarditis The chordae tendineae and left atrium and left ventricular endocardium are frequently involved by a spreading of the infection from the valve

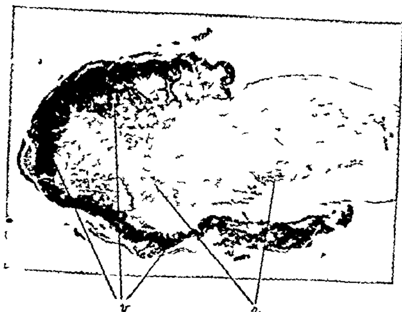


FIG 87 Microphotograph showing low power magnification of the cross section of the end of a cusp of the mitral valve infected by the Streptococcus viridans in subacute bacterial endocarditis Note vegetation (v) encircling the cusp end and consisting mostly of masses of bacteria and fibrin (stained black) Also note inflammatory leukocytic reaction (r) in the cusp itself



FIG 88 Photograph showing subacute bacterial (infective) endocarditis with vegetations on mitral valve and endocardium of left atrium (Kindness of Dr Ronald Grant, Guy's Hospital London)

cusps or by contact with the cusps that is, where the heart wall touches these vegetations on the cusp during the heart cycle The intima of the aorta may also be infected either where aortic valve vegetations are in contact with it or elsewhere An arteriovenous aneurysm may become infected by the Streptococcus viridans Finally congenital defects such as patent ductus arteriosus coarctation of aorta and especially interventricular septal defects and bicuspid aortic valves may be the site of invasion by the Streptococcus viridans

There may result from this inflammation of the endocardium an extension of the process into underlying tissues with deep ulceration or perforation or aneurysm formation in the valve cusps or local ulceration and aneurysm of the aorta (even with rupture) This type of aortic aneurysm like that resultin from acute bacterial endocarditis, is called a *mycotic aneurysm* In very rare cases the process may cause an aneurysm in or a perforation through the ventricular septum or from left ventricle into right atrium or even a rupture of atrial wall Also rarely invasion of the upper ventricular septal region may damage the atrioventricular bundle (of His) to cause heart block The vegetations sometimes grow very large or elongated and if this occurs on the aortic valve the vegetations may partially block the mouths of the coronary arteries

The valves of the left side of the heart are much more frequently involved than are those of the right side and the mitral valve oftener than the aortic though the great preponderance of mitral over aortic valve involvement seen in rheumatic heart disease does not hold here Pulmonary valve involvement is rare in subacute bacterial endocarditis in contrast to its involvement in acute bacterial endocarditis In a series of 90 autopsied cases of subacute bacterial endocarditis in which there was a specification of the valves that were involved in the process the mitral valve alone was affected in 25 the aortic valve alone in 18 both mitral and aortic in 38 mitral aortic and tricuspid in 2 all four valves in 1 pulmonary and aortic in 2 tricuspid and ventricular septal defect in 1 pulmonary and ductus arteriosus in 1 pulmonary aortic and ductus arteriosus in 1, and only the mural endocardium in the remaining 1 (Morrison 1932)

As already noted in the majority of cases Streptococcus viridans endocarditis is superimposed on chronic rheumatic valvular disease It is probable that in communities where rheumatic heart disease is infrequent the predisposing factor of congenital defects is as important as is that of rheumatic valvular disease and in such communities one would expect to find the total incidence of subacute bacterial endocarditis considerably reduced in comparison with that in rheumatic areas Out of 203 cases of subacute bacterial endocarditis analyzed in Boston 134 had clearly and others probably a rheumatic background 11 had congenital defects 3 an underlying syphilitic process and one a definite atherosclerotic basis (Morrison 1932) Markedly stenosed valves are less frequently attacked by subacute bacterial endocarditis the less slightly deformed valves in chronic rheumatic heart disease are the ones found at autopsy to be more often the site of this fatal complication and they are the ones which during life give rise to the murmurs of valvular regur

gitation (the systolic murmur of mitral origin at the apex and the diastolic murmur of aortic origin at the base)

Pericarditis in subacute bacterial endocarditis is rare but myocardial lesions have been reported (Bracht and Wachter 1909 Saphir 1946) consisting of diffuse inflammatory changes and of areas of infiltration in the interstitial tissue of the myocardium These areas however are also found in other cardiac infections and include the Aschoff body which may or may not indicate the presence of a coincident rheumatic heart infection in some cases Saphir has also described foreign body granulomas caused by calcific emboli arising from healed vegetations on the aortic valve in patients recently treated with penicillin or the sulfonamides

After recovery from subacute bacterial endocarditis the extent of chronic valvular disease may be increased Since however most of the valvular deformity is usually the result of previous rheumatic infection careful observation of the state of the heart before or at the onset of the subacute bacterial endocarditis is essential before it can be said that this disease caused or increased the valve deformity in a given case

Symptoms The symptoms of subacute bacterial endocarditis are like those of any infection but are less severe than in acute bacterial endocarditis Fever of varying grades occurs sometimes almost none at all and sometimes with wide daily swings of septic type as for example normal or subnormal temperature in the mornings and high fever (to 104° F or 40 C) in the evening Fever may however be absent for days at a time and then recur at intervals Chills and sweats are common Anorexia malaise prostration and loss of weight and strength are usual although for days or even weeks at the onset there may be merely a feeling of fatigue with little fever When embolism begins coming from thrombi in the heart local pain and other symptoms appear depending on the organ or the part of the body affected Splenic renal and cerebral infarctions are common With increasing anemia there may be hemorrhages into skin and from nose lungs and stomach—in addition to the embolic phenomena Finally if the disease is not brought under control the toxic state increases and weakness and mental confusion may become marked before death ensues or myocardial failure may develop with dyspnea or hepatic congestive pain or both if the infection is exhausting whether or not it is itself cured However with successful penicillin therapy at a relatively early stage of the disease nowadays, alert medical attention can in the majority of cases stop the process before any important complications take place

Signs The characteristic signs of the disease are fever a pallor due largely to secondary anemia and sometimes referred to as cafe au lait (Libman) petechial hemorrhages into the skin mucous membranes and conjunctivae splenomegaly clubbing of the fingers and evidence of valvular or congenital heart disease Rarely are all these signs pronounced in any given case usually the diagnosis must rest on two or three only generally supported however by a finding of the Streptococcus viridans by blood culture

The superficial *petechial hemorrhages* may be found anywhere on the body

and should be searched for carefully, they may be limited to the conjunctivae to the chest or elsewhere They are most commonly found on the forearms and hands, when located under the nails they are linear in shape and have been designated 'splinter hemorrhages They come and go often in crops in a given area, each spot rarely lasts more than a few days beginning as a small reddish or purplish dot under the skin not disappearing on pressure but gradually fading away within a week The spots vary in size usually from that of a pin point to that of the head of a large pin They may be produced in the forearm from the compression of the upper arm by a blood pressure cuff Thus they are evidently the result of damage to vessel walls by a toxin which allows leakage of blood whenever pressure trauma or some other factor favors it The petechiae are therefore related rather to a hemorrhagic tendency of which a common sign is nosebleed than to embolism Petechial hemorrhages although very common in subacute bacterial endocarditis are not pathognomonic of the disease they are also found not uncommonly in acute rheumatism

There is another sign of vascular origin often of value but not found in all cases of subacute bacterial endocarditis tender fingers and toes This is due most commonly to embolism of or hemorrhage from a small vessel in a finger tip or in a toe and consists of a deep painful purplish slightly swollen indurated area the size of a pea or smaller in the pulp of the end of the finger This lesion comes suddenly and disappears gradually in the course of a few days It may be isolated or there may be several such lesions at the same time or in succession Either fingers or toes may present this sign but more commonly the fingers are affected

The so-called Osler s node (Osler 1909) as described first by Mullen of Hamilton and later by Osler himself is a much rarer phenomenon it consists of a raised red nodule (never hemorrhagic) in the skin of finger or toe and not beneath it ½ to 1½ cm in diameter with a whitish point in the center and lasting a day or two

Still another sign and much the most important of those found in the fingers or toes of patients with subacute bacterial endocarditis is *clubbing* This condition also found in congenital heart disease and certain pulmonary diseases is shown in Figure 63 page 298 In subacute bacterial endocarditis it is very variable in occurrence and degree Clubbing is present in some measure in three quarters of all the cases but is well marked in only one half or somewhat less being most evident in the cases with enlarged spleens It does not appear at the onset of the disease but only when it is well advanced after the first few weeks Why it should occur in this disease has not been discovered but it is likely that local disturbance of the circulation (instead of general anoxemia with cyanosis as in congenital heart disease) causes capillary dilatation and increased soft tissue growth Instead of cyanosis there is usually increased redness of the bulbous finger tips When present clubbing is an important sign and should always be heeded but care must be taken not to confuse it with congenital or occupational abnormality of shape of the fingers Although the

toes may be clubbed as well as the fingers their clubbing is generally less obvious Clubbing recedes with recovery and disappears completely

Splenomegaly is common in subacute bacterial endocarditis and its presence is a very helpful sign However in about a third of the cases the spleen cannot be felt on physical examination Its enlargement when evident is usually not great, a firm nontender edge being felt just below the left costal border On rare occasions it may become large enough to extend almost to the umbilicus Like clubbing of the fingers splenomegaly usually clears up with recovery

The presence of evidence of *chronic valvular disease* or of *congenital defects* is usual and is somewhat corroborative One finds commonly an apical systolic murmur of mitral regurgitation occasionally the early diastolic murmur of aortic regurgitation and less commonly the murmurs of mitral stenosis aortic stenosis or congenital defects Sometimes an important murmur develops in the heart under observation indicating the onset or the increase of valvular deformity during this infection There is usually slight cardiac enlargement The heart may however appear normal on physical examination during most and rarely during all of the illness one may be misled thereby In such cases there may be endocarditis of a congenitally bicuspid aortic valve without enough actual valvular deformity to produce significant murmurs

Arrhythmia due to atrial fibrillation complicating subacute bacterial endocarditis was formerly thought to be extremely rare in recent years it has been found that their coexistence occasionally though still uncommonly takes place for example McDonald (1946) has reported 36 cases of atrial fibrillation (12 6 per cent) among 286 patients with subacute bacterial endocarditis Of these 36 cases 24 were carefully analyzed 3 showed paroxysmal arrhythmia and 21 permanent Of the 21 5 had the infection first, 6 had the arrhythmia first and 10 had both when first seen Premature beats are occasionally found but are of little importance The rare occurrence of delayed atrioventricular conduction (heart block) suggests extensive involvement of the interventricular septum Pericarditis is extremely rare in subacute bacterial endocarditis

Blood pressure roentgenologic and electrocardiographic studies show little or nothing abnormal except for evidence of underlying valvular disease congenital defect or heart block which may or may not be due to the subacute bacterial endocarditis

Blood studies are of much importance *Secondary anemia* is common if the disease lasts six weeks or more with red cell count between 3 and 3½ millions and hemoglobin at about 60 per cent somewhat lower figures of 2 to 3 millions of red cells and 40 to 50 per cent hemoglobin are also found but less frequently In rare cases the red count may drop to one million or less with hemoglobin of about 30 per cent A polymorphonuclear leukocytosis of slight to moderate degree (12 000 to 16 000) is common when there are complications such as embolism to spleen or elsewhere infrequently it is higher but more commonly it is lower often being recorded at a normal figure The blood smear shows achromia of red cells but only rarely polychromatophilia or change in size or shape of the cells The platelets are normal In a certain

small percentage of cases, perhaps 10 or 15 per cent, there are found in the blood smear occasional large endothelial phagocytic cells which are also found sometimes in other diseases their presence is somewhat helpful in corroborating the diagnosis The sedimentation rate is usually accelerated

Blood cultures carefully taken and repeated once or twice if necessary should be positive for the Streptococcus viridans in about 90 per cent of the cases A suitable culture medium is hormone broth with hydrogen ion concentration of *p*H 7 6 It is of interest to prepare pour plates in order to get some idea of the quantity of organisms by the number of colonies per plate which may vary from one to many Blood is collected in citrate flasks (½ cc of 4 per cent sodium citrate in a 50 cc Pyrex flask) from which 2 cc and two 1 cc samples are pipetted into tubes of melted nutrient agar which is cooled to 45 C after the tubes are rolled a few times the mixtures are poured into Petri dishes and the colonies are read after two and four days (kindness of Dr Louis Dienes) Cultures of venous blood usually suffice but on rare occasions cultures of bone marrow are positive when blood cultures are negative Arterial blood cultures are least satisfactory (Salazar Mallen, et al, 1947)

Titration of immune bodies in the blood in patients with subacute bacterial endocarditis has shown a high degree of such bodies much greater as a rule *than in the blood of the normal control* This test may perhaps prove helpful in establishing the diagnosis

The Wassermann reaction has sometimes been found positive in subacute bacterial endocarditis in the absence of syphilis this possibility should be remembered

The urine is not remarkable except for the frequent and important finding of numerous red blood corpuscles in the sediment There usually is not enough blood to appear macroscopically This finding in the sediment has been ascribed to renal infarction by multiple small emboli At postmortem examination glomerular lesions are frequently found (Baehr 1912) However it is probable that much of the blood in the urine is the result of minute hemorrhages comparable to those in the skin (petechiae) Albuminuria is commonly present if there is much fever or bleeding

Course and prognosis The gradual insidious onset of this disease often prevents any exact determination of the time of its beginning There may be a feeling of increasing fatigue and loss of appetite and sometimes there are vague joint and muscle pains the victim may appear pale listless and run down" for a few weeks before fever or other symptoms force him to bed or to ask for medical advice Months sometimes elapse with no definite idea of what is wrong Usually however in the early weeks of the illness the temperature reaction anemia enlarged spleen or clubbing of the fingers and heart signs and blood culture show the presence of this serious illness Prior to 1944 the symptoms and signs would steadily increase with development of embolic phenomena and death often the result of complications commonly ensued a few months to a year or more after the onset of the disease the average duration of the illness being about six months

Recovery prior to 1939 occurred in less than 1 per cent of all cases of subacute bacterial endocarditis rose to 5 or 6 per cent when the sulfonamides were introduced in maximal and very disagreeable dosage and five years later in 1944 abruptly increased to a little over 50 per cent with the advent of moderate but still inadequate amounts of penicillin Slowly in the five years that have elapsed since then when penicillin became available in larger and larger amounts and with increasing realization of the need of massive doses early in the disease and with the help of allies such as streptomycin at least 80 per cent of the patients have become curable It is likely that the ultimate figure will approach 90 but it is also probable that there will always be fatalities due to four causes (1) heart failure resulting from the extent of the heart disease itself plus the added strain of the infection and its treatment (2) embolism to brain or elsewhere and (3) intercurrent acute rheumatism these three causes operating even in cured patients and finally (4) resistance in a few cases to all specific therapy

It is to be remembered that a finding of the Streptococcus viridans in the blood by culture does not alone establish the diagnosis of subacute bacterial endocarditis even if chronic valvular disease (or a congenital cardiovascular defect) or fever is also present the presence of all three of these findings is however almost conclusive in a given case Positive blood cultures have been found without fresh endocarditis indicating that there is an illness of other nature present and not malignant endocarditis A preponderant group of signs should be present to establish the diagnosis of subacute bacterial endocarditis The clinical course is the most important clue For full reliance on blood cultures several (at least 3 or 4) should be found positive

There has been a very interesting small group of cases of subacute bacterial endocarditis mostly of historic interest now that became bacteria free but nevertheless went on for the most part to a fatal termination from uremia or heart failure they were characterized by the subsidence of fever negative blood cultures anemia brownish color of face and particularly severe glomerulonephritis (Libman 1913)

Finally advanced subacute bacterial endocarditis may be wholly or in large part symptomless prior to the occurrence of serious embolism which in the case of a woman 31 years old led rapidly to death from coronary occlusion (West 1931)

Complications The chief complications of this disease are due to infarction of various organs from emboli that arise from the intracardiac (chiefly valvular) thrombosis If these emboli are large and affect vital tissue a speedy death may follow The most important infarctions are those of the heart itself by coronary embolism of brain and of kidneys Cardiac infarction is very rare hemiplegia or paralysis of lesser extent is not uncommon after cerebral embolism and hematuria may result from renal infarction or simply from leaking blood vessels Hemorrhage of any serious moment is not often seen in this disease rarely it may complicate cerebral embolism and result fatally The renal damage may infrequently lead to uremia and death in a case of subacute

bacterial endocarditis A large embolus may obstruct an important artery to an extremity like the femoral popliteal tibial brachial or digital artery but rarely causes gangrene with need of amputation The spleen is one of the most common sites of infarction this explains the very frequent severe pain in the region of the spleen in patients with subacute bacterial endocarditis Mesenteric infarction may occur and it has been suggested that some pulmonary signs may be due to embolism of bronchial arteries Pulmonary infarction is not common inasmuch as the endocardial vegetations are generally or preponderantly on the left side of the heart but with thrombi in the right heart chambers this too can occur A long course of febrile illness in a patient with congenital heart disease affecting the right heart chambers complicated by pulmonary infarcts strongly suggests subacute bacterial endocarditis in such cases blood cultures may fail to show the Streptococcus viridans until late in the disease and clubbing of the fingers and splenomegaly may be wanting (Blumgart 1933)

Heart failure of congestive type is sometimes but not often *the cause of death* it is frequently present in slight or moderate degree brought on by the strain of infection and anemia in a heart already damaged rarely is there enough additional damage to the heart from this infection to cause failure directly Angina pectoris may rarely occur due to blocking of the mouths of the coronary arteries by the vegetations on the aortic valve, or to the added effects of aortic regurgitation and anemia Atrial fibrillation occurs infrequently and heart block appears in rare cases

Active rheumatism in the form of rheumatic fever or even of pancarditis may complicate subacute bacterial endocarditis apparently excited by it in some cases and pre-existing in others it was thought to be a complication in at least 17 and perhaps 4 more of Kelson and White s series of 250 cases (1945)

The secondary anemia itself if not well controlled by transfusion may become a grave complication favoring a fatal outcome In his weakened condition the patient may fall a victim to a complicating infection like pneumonia

Finally it is of some interest to note that pregnancy childbirth and the puerperium may progress without any material difficulty despite subacute bacterial endocarditis (Mengert 1933) although there may be Streptococcus viridans bacteriemia in the infant (Walser 1928)

Treatment In the first three editions of this book many different medicines and other empiric therapeutic measures were discussed but the only treatment that gave any promise at all was that with the sulfonamides especially sulfadiazine which was the least toxic while effecting rare cures When the sulfonamides were forced beyond the point of endurable toxic results there was a slightly higher percentage of recoveries Doses of 2 gm of a sulfonamide followed in two hours by another 2 gm initially and then 1 gm every four hours until the blood level reached close to 10 mg per 100 cc followed by adjustment of the dose to maintain that level in the course of a fortnight or two resulted

in a few cures Such supplementary therapy may still be of value when penicillin and streptomycin are alone or in combination ineffective Heparin and Dicumarol were added to this sulfonamide therapy in the early days with the thought that they might prevent the deposition of new thrombi on the endocardium while those already present were being sterilized but practical experience during recent years has indicated that such addition to the treatment has not resulted in any gain and instead has been troublesome expensive and even on occasion harmful

It is of historic interest merely to insert herewith without further comment except to note their failure the imposing list of drugs and other therapy tried years ago in the vain effort to cure this dread disease arsenic in various forms mercury gentian violet salicylates antiseptics of all kinds vaccines serums transfusions including those from immunized donors production of sterile abscesses splenectomy electrotherapy diathermy and hyperthermia A few of these measures have had on occasion a somewhat helpful though not curative effect transfusions have so acted when there has been a severe anemia and both splenectomy and hyperthermia have had their advocates

Happily today one can be brief and explicit about therapy that is effective in the great majority of cases as the result of the discovery reported by Fleming in 1929 that Penicillium notatum a common mold contained a potent antibacterial substance of its purification and application by Florey and his colleagues in 1940 and of its curative effect in subacute bacterial endocarditis by Loewe in 1944 After the diagnosis has been established as early in the disease as possible or if not proved at least considered probable after careful study penicillin should be administered at once in adequate dosage and continued as a rule for six weeks with a range of four to eight, or as much longer as may be deemed necessary in any particular case A dose of 500 000 to 1 000 000 units a day should be given parenterally if for any reason oral medication is given the daily dose must be 5 to 10 times greater to produce the same beneficial effect If after a week or ten days there is no obvious effect of the 500 000 to 1 000 000 unit dose on fever clinical course or blood culture the daily amount should be multiplied five times Even as much as 20 000 000 units a day for weeks has been necessary to effect a cure in rare cases

Common mistakes quite natural in the early days of such therapy because of the limited supply of the penicillin were to give too little at the start and to increase the size of the dose too slowly and too cautiously It is far wiser to give a larger amount than may be necessary at the beginning rather than to allow the infection to continue too long with the hazard of serious complications It is however best of all routinely to adopt the procedure of in vitro testing of the sensitivity to penicillin of the causative organism whether Streptococcus viridans or not since there has been shown to be a very definite relationship between this sensitivity and the curative dosage (Hunter 1946 Clark et al 1948) The great majority of the strains of the Streptococcus viridans are inhibited by 0 1 unit of penicillin per cubic centimeter of culture

medium and so do not need maximal dosage but a few require 0 2 to 0 5 units and a very few up to 1 unit or more It has been helpfully advised that for the first that is the more sensitive group a daily dose of 500 000 units be given for the second that is the intermediate group a dose of 1 to 2 million units, and for the third the most resistant group a dose of 5 to 20 million units a day If these maximal doses are still ineffective adjuvant treatment with caronamide or streptomycin is in order (see below)

Various methods of administration of the penicillin have been introduced and they all have had their advocates as may be found on consulting the Bibliography of this chapter Intramuscular injections in sterile saline or aqueous solution every two to four hours (usually three) day and night were in use most frequently and proved to be quite practical and effective Constant intramuscular and intravenous drips were also curative earlier and had the advantage of producing a more constant blood level but the disadvantage of inconvenience Penicillin in oil and beeswax proved helpful in establishing a fairly uniform absorption and blood concentration although without high levels (Hewitt 1947 Hoffman et al 1947) this procedure was especially convenient because it reduced the number of injections needed intramuscularly to two in twenty four hours and was recommended in particular for prophylaxis as in the case of dental extractions Recently there has come into more or less routine use a preparation of penicillin with procaine (which has a beneficial twofold effect of rendering the injection painless and slow in absorption) which can be very conveniently and effectively injected intramuscularly in the dosage of 300 000 or 600 000 units every six hours giving satisfactory total daily doses of 1 200 000 or 2 400 000 units respectively

Another important means of maintaining a more or less uniform and especially a higher (threefold or more) concentration of penicillin in the blood particularly useful in obstinate cases not responding well to lower concentrations is by adding caronamide or benemid which blocks the ordinarily rapid excretion of penicillin through the renal tubules (Beyer 1947 Boger et al 1947 1949 and 1950 Loewe et al 1947 Meads et al 1948 Burnell and Kirby 1951) Four grams of caronamide are given orally every three to four hours or ½ gm of benemid every six hours for days to weeks in order to produce a blood serum concentration of approximately 30 mg per 100 cc which is necessary in order to maintain a threefold or more increase of penicillin level The drug must be used with some caution however in patients who have any suspicion of reduced kidney function beforehand and probably not at all when serious kidney disease is present Also toxic symptoms such as nausea and vomiting may be induced in some cases However the use of caronamide and benemid has resulted in cures by penicillin in cases not responding well without it

Finally in cases fortunately very few in number in which penicillin is ineffective it may be necessary to resort to streptomycin alone or in addition or even to add sulfadiazine This applies to organisms particularly gram negative bacilli and certain gram positive cocci which are very insensitive to

penicillin In such cases after the in vitro and brief in vivo testing with penicillin and in vitro testing with streptomycin the latter should be injected intramuscularly in the dosage of 0 5 to 1 0 gm (preferably the larger dose) every six hours for days to weeks depending on the clinical progress and toxic symptoms This gives a blood concentration of streptomycin of some 10 to 20 units (or micrograms) per 100 cc which is as a rule far greater than the in vitro sensitivity of the organism causing the disease There are two difficulties which render streptomycin much less satisfactory to deal with than penicillin (1) the toxic effects which include especially vertigo which may be permanent secondary to labyrinthitis fever dermatitis and pruritis and (2) increasing resistance of the organism to the drug Despite these disadvantages there are well-established cures of subacute bacterial endocarditis by streptomycin Much more rarely and more or less as a last resort sulfadiazine may be added to penicillin or streptomycin or both in the oral dosage of 4 gm initially or 2 gm repeated in two hours followed by 1 gm every four hours until the blood level reaches 10 mg per 100 cc with continuation at that level and finally other antibiotics besides penicillin are worthy of trial in the case of unusual and rare infectious agents not amenable to penicillin

Mention should be made of course of the importance of the best nursing care in the treatment of this disease of patient but optimistic attitude of both doctor and victim during the tedious weeks of therapy and of the early recognition and treatment of complications such as congestive heart failure by the use of digitalis low sodium intake and diuretics In very rare cases cure of infected peripheral blood vessels as in instances of mycotic and arteriovenous aneurysms has been effected by surgical excision

Differential diagnosis The four conditions from which it may be difficult to differentiate subacute bacterial endocarditis are (1) active rheumatic heart disease (2) acute bacterial endocarditis (3) infections of other nature with or without chronic valvular disease and (4) blood diseases or severe anemia secondary to some other infection like malaria The duration and average severity of subacute bacterial endocarditis the relative infrequency and unimportance of joint pains or swelling the clubbing of the fingers when present the slight but usually not great enlargement of the spleen the moderate grade of secondary anemia the finding of the Streptococcus viridans in the blood stream and particularly the frequency of embolism in an infection not very virulent in nature distinguish this disease with little difficulty from others It is however important to remember that the various conditions cited above may coexist in the same case

BIBLIOGRAPHY

ACUTE AND SUBACUTE BACTERIAL (INFECTIVE) ENDOCARDITIS
MALIGNANT ENDOCARDITIS

Acute Bacterial Endocarditis

Fox W W Endocarditis Due to the Hemolytic Para influenza Bacillus" *J A M A* 1935 CV 876
Gelfman R and Levine S A Incidence of Acute and Subacute Bacterial Endocarditis in Congenital Heart Disease *Am J M Sc* 1943 CCIV 324
Goldburgh A L Baer S and Lieber M M "Acute Bacterial Endocarditis of the Tricuspid Valve" *Am J M Sc* 1942 CCIV 319
Hurwitz A and Arst D B Mycotic Aneurysm of the Brachial Artery After Cure of Bacterial Endocarditis *New England J Med* 1948 CCXXXVIII 903
Hussey H H et al "Septicemia and Bacterial Endocarditis Resulting from Heroin Addiction Report of Five Cases *J A M A* 1944 CXXVI 535
Lion G and Levy Bruhl M Un cas d endocardite infectieuse gonococcique avec serodiagnostic positive *Arch d mal d coeur* 19_2 XV 289
Locke E A "Pneumococcus Endocarditis *Boston M and S J* 1924 CXCI 913
Lord F T "Pneumococcus Endocarditis *New England J Med* 1932 CCVII 767
Luttgens W F Endocarditis in Main Line Opium Addicts Report on Eleven Cases *Arch Int Med* 1949 LXXXIII 653
Menetrier Releve statistique de 400 autopsies de pneumonie *Bull et mem d soc med d hop d Paris* 1919 XLIII 679
Merritt W A "Bacterial Endocarditis as Complication of Transurethral Prostatic Resection" *J Urol* 1951 LXV 100
Mulson F W and Hess H R "Acute Bacterial Endocarditis in Infants" *Am Heart J* 1936 XII 368
Phipps C "Acute Bacterial Endocarditis *New England J Med* 1932 CCVII 768
Rhoads C P "Vegetative Endocarditis Due to the Meningococcus with a Case Report. *Am J Path* 1927 III 623
Robinson G L, and Hartley R Acute Bacterial Endarteritis" *Brit Heart J* 1951 XIII 106
Ruiz F R and Garcia P P "Infeccion puerperal y endocarditis maligna *Rev med latino-am* Buenos Aires 1926 XI 2053
Russell D S and Fildes P A Case of Endocarditis in Man Associated with Bacillus Parainfluenzae Rivers 1922 *J Path & Bact* 1928 XXI 651
Sheldon W H and Golden A "Abscesses of the Valve Rings of the Heart A Frequent But Not Well Recognized Complication of Acute Bacterial Endocarditis" *Circulation* 1951 IV 1
Thayer W S "On the Cardiac Complications of Gonorrhoea *Bull Johns Hopkins Hosp* 1922 XXXIII 361
"Observations on Bacterial Endocarditis" *Weekly Roster and Medical Digest* Philadelphia Mar 14 1925 XX 17
Warfield L M "Acute Staphylococcus Aureus Endocarditis" *Am Heart J* 1927 II 576
Williams R H Gonococcic Endocarditis Study of Twelve Cases with Ten Postmortem Examinations" *Arch Int Med* 1938 LXI 26

Subacute Bacterial Endocarditis

Abbott M E *Atlas of Congenital Cardiac Disease American Heart Association* New York 1936
Baehr G "Glomerular Lesions of Subacute Bacterial Endocarditis" *Tr A Am Physicians* 1912 XXVII 177
Blumer G "Subacute Bacterial Endocarditis" *Medicine* 1923 II 105
Blumgart H L "The Clinical Syndrome of Subacute Bacterial Endocarditis Involving the Right Chambers of the Heart" *M Clin North America* 1933 XVI 881

Bracht E and Wachter "Beitrag zur Atiologie und pathologischen Anatomie der Myocarditis rheumatica *Deutsch Arch f klin Med* 1909 XCVI 493

Chain E Florey H W Gardner A D Heatley N G Jennings M A Orr Ewing J and Sanders A G Penicillin as a Chemotherapeutic Agent *Lancet* 1940 II - 6

Fleming A "The Antibacterial Action of Cultures of Penicillin with Special Reference to Their Use in Isolation of B influenzae *Brit J Exper Path* 1929 X 236

Galbreath W R and Hull E "Sulfonamide Therapy of Bacterial Endocarditis Results in 4 Cases *Ann Int Med* 1943 XVIII 201

Gelfman R and Levine S A Incidence of Acute and Subacute Bacterial Endocarditis in Congenital Heart Disease *Am J M Sc* 1942 CCIV 324

Goetsch C Persistent Ostium Atrio Ventriculare Commune with Bacterial Endocarditis in a Mongolian Idiot *J Tech Methods* 1938 XVIII 117

Grant, R T Wood J E Jr and Jones T D "Heart Valve Irregularities in Relation to Subacute Bacterial Endocarditis *Heart* 1928 XIV 247

Hamman, L and Rienhoff W F Jr Subacute Streptococcus Viridans Septicemia Cured by Excision of an Arteriovenous Aneurysm of External Iliac Artery and Vein *Bull Johns Hopkins Hosp* 1935 LVII 219

Heyman J "Subacute Bacterial Endocarditis Successfully Treated with Sulfanilamide Report of Well Established Case 18 Months After Recovery" *J A M A* 1940 CXIV 23 3

Kelson, S R and White P D "A New Method of Treatment of Subacute Bacterial Endocarditis Using Sulfapyridine and Heparin in Combination *J A M A* 1939 CXIII 1700

Lewis T and Grant R T Observations Relating to Subacute Infective Endocarditis Part 1 Notes on the Normal Structure of the Aortic Valve Part 2 Bicuspid Aortic Valves of Congenital Origin Part 3 Bicuspid Aortic Valves in Subacute Infective Endocarditis *Heart* 1923 X 21

Libman E "The Clinical Features of Cases of Subacute Bacterial Endocarditis That Have Spontaneously Become Bacteria Free *Tr A Am Physicians* 1913 XXVIII 309

"The Clinical Features of Sub acute Streptococcus (and Influenzal) Endocarditis in the Bacterial Stage *M Clin North America* 1918 II 117

Libman, E and Friedberg C K *Subacute Bacterial Endocarditis* Oxford University Press New York 1941

Martin H F and Adams W L Jr "Bacterial Endocarditis Superimposed on Syphilitic Aortitis and Valvulitis" *Am Heart J* 1938 XVI 714

Mengert W F "Subacute Bacterial Endocarditis as Complication of Pregnancy" *Am J Obst & Gynec* 1933 XXV 121

Morrison H "A Study of the Incidence of Subacute Bacterial Endocarditis at the Massachusetts General Hospital" *Boston M and S J* 1927 CXCVII 46

Subacute Streptococcus Endocarditis" *New England J Med* 1932 CCVII 770

Okell C C and Elliott S D Bacteriaemia and Oral Sepsis with Special Reference to Aetiology of Subacute Bacterial Endocarditis" *Lancet* 1935 II 869

Orgain F S and Foston M A "Mixed Infections in Bacterial Endocarditis" *Am Heart J* 1942 XXIII 823

Osler W "Infectious (so-called Ulcerative) Endocarditis" *Arch Med* 1881 V 44

Chronic Infectious Endocarditis *Quart J Med* 1909 II 219

Palmer H D and Kempf M Streptococcus Viridans Bacteriemia Following Extraction of Teeth" *J A M A* 1939 CXIII 1788

Parks H "An Instance of Coronary Embolism in Subacute Bacterial Endocarditis" *Ann Int Med* 1942 XVI 339

Rost W L and Fischer A E "Subacute Bacterial Endocarditis in Childhood Report of 12 Cases *Am J Dis Child* 1928 XXXVI 1144

Schottmuller H "Endocarditis lenta zugleich ein Beitrag zur Artunterscheidung der pathogenen Streptokokken *Munch med Wchnschr* 1910 LVII 617

Smith C, Sauls H C and Stone C F "Subacute Bacterial Endocarditis Due to Streptococcus Viridans A Survey of the Present Status of the Previously Reported Cures and a Clinical Study of 15 Treated Cases, Including Another Cure" *J A M A* 1942 CXIX, 478

Touroff A S W and Vessell H Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus Recovery Following Surgical Treatment. *J A M A* 1940 CXV 1270

Walser H C "Subacute Bacterial Endocarditis of Streptococcus Viridans Type in Pregnancy with Two Case Reports *Am J Obst & Gynec* 1928 XV 840

Weiss H Relation of Portals of Entry to Subacute Bacterial Endocarditis" *Arch Int Med* 1934 LIV 710

West G L Sudden Death in a Case of Asymptomatic Subacute Bacterial Endocarditis. *New England J Med* 1931 CCV 675

White P D and Jones T D Heart Disease and Disorders in New England *Am Heart J* 1928 III 302

Willius F A Cardiac Clinics LXX Clinic on Subacute Bacterial Endocarditis Affecting an Aged Patient *Proc Staff Meet Mayo Clin* 1940 XV 270

Recent References (1944–1950)

Aubert A and Lerche C Subacute Bacterial Endocarditis in a Child Ten Months Old Successfully Treated with Streptomycin *Am Heart J* 1950 XXXIX 141

Beyer K H New Concept of Competitive Inhibition of the Renal Tubular Excretion of Penicillin *Science* 1947 XCV 94

Boger W P et al The Influence of a New Benzoic Acid Derivative [Benemid] on the Metabolism of Para aminosalicylic Acid (PAS) and Penicillin" *Ann Int Med* 1950 XXXIII 18

Boger W P Kay C F and Eisman S H and Yeoman E E Caronamide Compound That Inhibits Penicillin Excretion by Renal Tubules Applied to Treatment of Subacute Bacterial Endocarditis *Am J M Sc* 1947 CCXIV 493

Burke F G Ross S Walsh B J and McLendon P A "Successful Use of Oral Penicillin in Treatment of Subacute Bacterial Endocarditis Report of Case *M Ann District of Columbia* 1946 XV 22

Burnell J A and Kirby W M M 'The Effectiveness of the New Compound Beremid in Elevating Serum Penicillin Concentrations *J Clin Investigation* 1951 XXX 697

Christie R V Penicillin in Subacute Bacterial Endocarditis Report to Medical Research Council on 269 Patients Treated in 14 Centres Appointed by Penicillin Clinical Trials Committee *Brit M J* 1948 I 1

Clark W H Bryner S and Rantz L A Penicillin resistant Non hemolytic Streptococcal Subacute Bacterial Endocarditis" *Am J Med* 1948 IV 671

Cunningham W D and Maddox K Cure of Subacute Bacterial Endocarditis During Pregnancy Report of a Case *M J Australia* 1949 II 391

Dawson M H and Hunter T H "The Treatment of Subacute Bacterial Endocarditis with Penicillin Second Report *Ann Int Med* 1946 XXIV 170

Dreher H S Jr Subacute Bacterial Endocarditis Due to Streptococcus Fecalis Failure of Massive Prolonged Penicillin Treatment Case Report with Autopsy" *Kansas M Soc J* 1950 LI 119

Eisman S H Kay C F Norris R F and Boger W P Caronamide as an Adjuvant to Penicillin in the Treatment of Subacute Bacterial Endocarditis *Am J M Sc* 1949 CCXVII 62

Glaser R J Dankner A Mathes S B and Harford C G "Effect of Penicillin on the Bacteremia Following Dental Extraction" *Am J Med* 1948 IV 55

Hart F D Morgan A and Lacey B "Brucella Abortus Endocarditis *Brit M J* 1951 I 1048

Hewitt W L "Serum Concentrations of Penicillin Following Administration of Crystalline Penicillin G in Peanut Oil and Beeswax" *Am Practitioner* 1947 II 247

Hoffman W S Volini I F and Hughes J R "Treatment of Subacute Bacterial Endocarditis with Penicillin in Oil and Beeswax" *J Lab & Clin Med* 1947 XXXII 1529

Hunter T H "Treatment of Subacute Bacterial Endocarditis" *Mod Concepts Cardiovas Dis* 1946 XV No 8

Hurst W W Gleason A L and Schemm F R "Subacute Bacterial Endocarditis after Operation for Tetralogy of Fallot" *Northwest Med* 1949 XLVIII 763

Jones M Subacute Bacterial Endocarditis of Nonstreptococcic Etiology A Review of the Literature of the Thirteen Year Period 1936–1948 Inclusive *Am Heart J* 1950 XL, 106

Kaplan S R Rosenman R H Katz L N and Brams W A Healed Subacute Bacterial Endocarditis A New Entity *J.A.M.A* 1949 CXLI 114

Keefer C S Anderson D G and Hewitt W L End Results in the Treatment of Bacterial Endocarditis *Tr A Am Physicians* 1948 LXI 112

Keefer C S and Hewitt W L "Bacterial Endocarditis Report of End Results in Thirty nine Patients *Boston M Quart* 1950 I 1

Kelson S R and White P D "A Review of 250 Cases of Subacute Bacterial Endocarditis in Boston Hospitals from 1927 to 1939 *Ann Int Med* 1945 XXII 40

Latscha, B Lenegre J and Mathivat A "Un cas d embolie et un cas d occlusion ostiale coronariennes au cours de l endocardite maligne lente *Arch d mal du coeu* 1949 XLII, 729

Levy L. and Hull E "Perforation of the Interventricular Septum in a Case of Subacute Bacterial Endocarditis *Am Heart J* 1947 XXXIII 856

Littmann D., and Schaaf R S Therapeutic Experiences with Subacute Bacterial Endocarditis Reference to the Failures" *New England J Med* 1950 CCXLIII 248

Loewe L. Rosenblatt P Greene H J and Russell M Combined Penicillin and Heparin Therapy of Subacute Bacterial Endocarditis *J A M A* 1944 CXXIV 144

Loewe L Eiber H B and Alture Werber E Enhancement of Penicillin Blood Levels Following Oral Administration of Caronamide *Science* 1947 CVI 494

M Donald R K. "The Coincidence of Auricular Fibrillation and Bacterial Endocarditis" *Am Heart J* 1946 XXXI 308

MacLean H and Howell K M "Two Coexistent Strains of Viridans Streptococcus Isolated from Blood Cultures by Penicillin Sensitivity Tests *Am J M Sc* 1947 CCXIV 53

Meads M Long R V Pace S H and Harrell G T Caronamide and Penicillin *J A M A* 1948 CXXXVIII 874

Mendelson C L Pregnancy and Subacute Bacterial Endocarditis *Am J Obst & Gynec* 1948 LVI 645

Olinger M G "Mixed Infection in Subacute Bacterial Endocarditis Report of Two Cases" *Arch Int Med* 1948 LXXXI 334

Orgain E S and Donegan C K "The Treatment of Bacterial Endocarditis *Ann Int Med* 1950 XXXII 1099

Paul O Bland E F and White P D "Bacterial Endocarditis Experiences with Penicillin Therapy at the Massachusetts General Hospital 1944–1946" *New England J Med* 1947 CCXXXVII 349

Pulaski E J and Connell J F Jr Procaine Penicillin G for Aqueous Injection A Study of Blood and Urine Levels" *New England J Med* 1949 CCXLI 514

Roston E H and Stollerman G H Procaine Penicillin in the Treatment of Subacute Bacterial Endocarditis *Am Practitioner* 1949 IV 102

Salazar Mallen M Lozano Hube E and Brenes M Comparative Study of Blood Cultures Made from Artery Vein and Bone Marrow in Patients with Subacute Bacterial Endocarditis *Am Heart J* 1947 XXXIII 692

Saphir O "Myocardial Granulomas in Subacute Bacterial Endocarditis *Arch Path* 1946 XLII 574

Saphir O Katz L N and Gore I The Myocardium in Subacut Bacterial Endocarditis *Circulation* 1950 I 1155

Spies H W Dowling H F Lepper M H and others "Aureomycin in Treatment of Bacterial Endocarditis Report of Nine Cases Together with Study of Synergistic Action of Aureomycin and Penicillin in One Case" *Arch Int Med* 1951 LXXXVII 66

Taniguchi T and Murphy F D "Mural Bacterial Endocarditis Produced by Proteus *J.A.M.A* 1950 CXLIII 427

Traut E F Carter J B Gumbiner S H and Hench R N "Bacterial Endocarditis in the Elderly A Report of 94 Autopsied Cases *Geriatrics* 1949 IV 205

Zeman F D Subacute Bacterial Endocarditis in the Aged" *Am Heart J* 1945 XXIX 661

CHAPTER 16

CARDIOVASCULAR SYPHILIS

Introduction This is another chapter which we may justifiably hope and expect to become obsolete during the next generation since already great progress in the reduction of cardiovascular syphilis has been actually demonstrated to the author and his contemporaries during the past generation by means of the prevention of syphilis itself in the first place its earlier recognition and more adequate initial treatment in the second place and its better therapy even in its later or tertiary phase in the third place

In every chapter that has preceded the present one a considerable revision has been necessary as the result of the rapid strides of medical progress in the past seven years since the last edition of this book Even more dramatically has progress been *made in the subject of the present chapter* in the way of preventive medicine And yet despite this advance syphilis continues to be after rheumatism the second most common and important cause of infectious cardiovascular disease By the time the diagnosis of cardiovascular syphilis is made it is in most cases a very serious condition Fortunately however it is a preventable disease and already in many parts of the world it is on the wane *and no longer common In New England two decades ago it was found* to make up 4 per cent of a large series of cases of cardiovascular disease (White and Jones 1928) being more frequent in general hospital practice than in private practice now however it makes up less than a quarter of that figure (that is less than 1 per cent) Among the Negroes in the southern part of the United States on the other hand it is still a common though decreasing cause of cardiovascular disability and death being a prime factor in about 20 per cent of cardiac patients even there it is less frequent than the factor of hypertension In a series of 414 Negroes in Texas with cardiovascular disease over twenty years ago syphilis was the chief factor in 32 per cent and hypertension in 50 per cent (Stone and Vanzant 1927) there too however the recent public health campaign gives promise of a reduction in cardiovascular syphilis, such as has occurred elsewhere

It is a very interesting fact as yet unexplained that syphilis damages the

aorta more than other arteries or the myocardium Cardiovascular syphilis consists primarily therefore of aortitis with or without secondary effects on the heart infrequently it means myocardial disease or involvement of great vessels other than the aorta such as the femoral carotid and pulmonary arteries

In a series of 50 000 consecutive autopsies in Minnesota over a period of thirty seven years beginning in 1910 syphilitic heart disease not including uncomplicated aortitis dropped in incidence from a maximum of 2 04 per cent at the beginning to 0 23 per cent at the end in individuals 40 years of age or older (Clawson 1950) the general incidence of syphilitic cardiac deaths (0 83 per cent) in this autopsy material is now less than that of deaths from calcific aortic valvular disease (1 3 per cent) Syphilitic aortic insufficiency ranked first in the manner of death in Clawson s series of cases of syphilitic heart disease (58 5 per cent) Deaths due to rupture of a syphilitic aneurysm were second with 21 per cent and those due to narrowing of the coronary orifices third with 18 9 per cent There were relatively few cases of gumma of the myocardium

In a series of 9 807 necropsies in Italy the incidence of heart disease due to syphilis was found to be 2 per cent (Venzoni 1939) in a Cincinnati hospital with a large proportion of Negro inmates however the incidence of syphilitic aortitis in autopsies from 1926 to 1937 inclusive was reported to be much higher (at least 9 1 per cent) (Gelperin 1940) while in the Philadelphia General Hospital the percentage dropped from 9 2 in the years 1927 to 1930 to 5 6 in 1935 to 1937 (there was a majority of Negro cases) (Welty 1939)

Etiology *Cause* The organism responsible for cardiovascular syphilis the Treponema pallidum was discovered in a diseased aorta in 1906 (Reuter) but long before the discovery of the actual causative agent in syphilis the connection between that disease and aortitis was known and for several centuries the production of aneurysms by syphilis was suspected (Pare 1575 Lancisi 1724, and Morgagni 1761) Gummata long known to be of syphilitic origin were early found in the heart itself

Although it is probable that the spirochete of syphilis invades the heart and aorta early in the disease at the same time that it invades other organs actual disease of aorta and of heart due to syphilis is as a rule first demonstrable either by symptoms or by signs only a good many years after the primary lesion (chancre) Twenty years elapse on the average between the onset of the infection and its evident involvement of the cardiovascular apparatus but there are wide variations the intervals ranging from a few weeks to 30 or 40 years Except in rare cases clear evidence is wanting that there is any important involvement of the heart or aorta during the primary or secondary stage (that is during the first few weeks or months) of the syphilitic infection most reports to the contrary are unsatisfactory Years ago because of the lateness of this evidence of infection aortitis and aneurysms were classed along with tabes dorsalis and general paresis as fourth stage or parasyphilitic lesions

that is the end result of the infection that had become inactive while gummata when they were found were considered manifestations of the tertiary stage still active Now we know that all these processes are but different evidences of the syphilitic infection appearing late but still active, a few aneurysms are relatively inactive scarred lesions but such unprogressive aneurysms are uncommon

There is obviously some sort of affinity between the treponema and the aortic wall just as there is between this organism and the central nervous system in certain individuals, what it is we do not yet know Most cases of acquired syphilis do not however develop cardiovascular disease at least 90 per cent never show clinical or pathologic evidence of such involvement.

Congenital syphilis as well as acquired syphilis may cause cardiovascular disease but the congenital syphilitic type is not common The simple presence of treponemata in the heart muscle of a syphilitic fetus or child (a common finding at postmortem examination) does not constitute syphilitic heart disease there must be appreciable tissue reaction or destruction in addition This is well illustrated by a report of a study of 939 children with congenital syphilis (McCulloch 1930) 498 of these children were over two years of age and only 5 showed any signs of cardiovascular disease and in them such heart disease was clearly of rheumatic nature of the other 441 children who were under two years of age 32 died but only 3 of these were found to have syphilitic heart disease while none of the 409 survivors showed any signs whatsoever of cardiovascular syphilis

Age Because of the possibility of cardiovascular involvement by syphilis in fetal life and of the possible acquisition of the infection relatively late in life the age at which cardiovascular syphilis may show itself clinically or at autopsy varies from birth to old age The usual age of clinical manifestation however is in the late forties the large majority of cases come to notice between the ages of 40 and 55 years In one series of 95 cases there was one patient less than 10 years old there were four between the ages of 20 and 30 eleven between 30 and 40 twenty five between 40 and 50 thirty three between 50 and 60 twenty between 60 and 70 and one over 70 (White and Jones 1928) Among Negroes the age at which cardiovascular syphilis becomes evident is younger nearer 40 than 50 frequently in the thirties and even rarely in the twenties In recent years two more cases with syphilitic thoracic aneurysms who were under the age of 30 years have been reported (Evans 1941)

Sex The male sex has far more cardiovascular syphilis than has the female In the series of 95 cases mentioned above 78 were male and 17 were female a ratio of almost 5 to 1 (White and Jones 1928) In another series of 70 cases the ratio was 6 to 1 (Nichols 1940) In Moore s series the ratio was about 2 to 1 (Moore et al 1932) and in a more recent series of 199 cases of syphilitic aortitis found among 9 807 necropsies (Venzoni 1939) there were 164 men and 34 women (5 to 1) This is undoubtedly due largely

to the far greater male exposure to syphilis and to the factor of greater physical activity

Other factors Other known etiologic factors in cardiovascular syphilis are *race* and *social and economic status* These are very important since the members of most of the less civilized races are far more subject to syphilis once it is introduced among them than are those of civilized races where social customs and measures of prevention and early treatment afford at least a certain amount of protection Even in a civilized community the percentage of cardiovascular syphilis is greater among the inhabitants of lower social and economic order In Moore s series it was about twice as common in Negro as in white patients (Moore et al 1932) A large percentage of the population of some half civilized peoples is found to be infected with syphilis what percentage of those develop cardiovascular disease due to this infection we do not know because of the lack of accurate statistics we might at first thought believe that cardiovascular syphilis would be very common in such peoples but that is not always the case as found out in Arabia by Paul Harrison (personal communication 1940) who encountered only very rare cases of aortic aneurysm or aortic regurgitation in an active medical service over many years in a country riddled with syphilis It seems likely that a relative immunity so far as serious effects are concerned can be acquired in countries where syphilis has long been almost universal and but little treated In Uganda however cardiovascular syphilis is said to be common comprising over half of all heart disease among Africans (Williams 1938)

The more laborious occupations are also almost certainly a cause for early appearance and rapid evolution of aortic changes due to syphilis because of the greater physical strain produced thereby

The factor of early and satisfactory treatment of the original syphilitic infection is undoubtedly one of much importance as it concerns the later development of cardiovascular disease of syphilitic origin in civilized communities at least This is only now becoming evident since it is only in recent years that antisyphilitic therapy has been planned and administered in any satisfactory degree to the majority of patients An example of this effect is the decrease in the incidence of cardiovascular syphilis both relatively and absolutely seen at the Massachusetts General Hospital in recent years In 1914 Cabot reported 12 per cent of a group of 600 cardiac cases as due primarily to syphilis in 1928 White and Jones reported 5 per cent of a series of 880 cardiac cases as primarily or secondarily of this type in the same clinic while in 1949 we have found only 1 5 per cent among 1 000 cardiac cases another interesting comparison in this hospital is that of the incidence of the diagnosis of aneurysm of the aorta in the ten year period of 1900 to 1909 inclusive (113 among 51 875 cases or 0 2 per cent) with that in the ten year period of 1925 to 1934 inclusive (only 61 among 75 184 cases or 0 08 per cent despite the improved roentgenologic facilities for diagnosis) In Baltimore in 1932 Moore and his associates stated that not one of 117 patients with

early syphilis who received three or more courses of arsphenamine and tr
ment with mercury during periods between the courses presented any
dence of cardiovascular involvement during the period of observation (u
nine years after the infection) while 24 of 285 patients followed during
same period of observation who had received less than this amount of tr
ment were observed to acquire syphilitic aortitis aneurysm or aortic
gurgitation Adequate treatment for early syphilis almost certainly protects
majority of patients so treated against subsequent cardiovascular syphi
Various procedures are now in progress in the use of penicillin in the r
treatment of early syphilis for example 600 000 units of procaine penic
daily for ten days (Kossmann personal communication 1949)

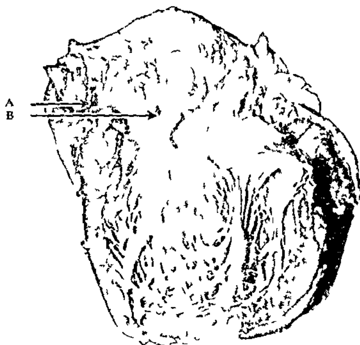


FIG 89 Photograph showing syphilitic aortitis with marked narrowing of the mo
of the right coronary artery (*B*) the mouth of the left coronary artery (*A*) is sligh
narrowed Compare this with Figure 14? (Jores *Arterien* Courtesy of Julius Spring
Berlin)

Pathology Cardiovascular disease due to syphilis is of three main typ
1 The first and commonest type is the result of *destruction of the med* *of arteries* The exact pathogenesis of this lesion is not known in the aor
it is thought to result from obliterative endarteritis of the vasa vasorum It
most evident in the ascending portion of the aorta where the intima becom
pale and wrinkled due to the destruction of the media below it (Figure 89
The aortic wall is thus seriously weakened and loses its elasticity stretch
and dilates The intima is thickened becomes atheromatous and may ulcerat

though ulceration is less common than in the case of primary atheroma The spirochete of syphilis may sometimes be found in the diseased aorta

Three important developments of this destructive syphilitic aortic process may occur if no one of these is found as sometimes happens the condition then remains clinically unimportant These three developments are (1) a stretching of the aortic wall to give rise either to a diffuse or spindle shaped dilatation or aneurysm or locally to a saccular aneurysm (2) an involvement of the aortic valve to deform it and to cause aortic regurgitation and (3) a narrowing of the mouths of important branches of the aorta by an extension of the process itself

(a) *Aortic aneurysms* like syphilitic aortitis itself most commonly involve the ascending portion of the aorta less often the aortic arch and least often the descending portion in thorax or in abdomen They are only an occasional accompaniment of aortitis being found in 10 per cent or fewer of the cases but they are serious because of the pressure they often exert on surrounding structures and because of their tendency to rupture into pleural cavities pericardial sac bronchi or trachea esophagus mediastinum or even into other great vessels (pulmonary artery or superior vena cava) Aneurysms are still rarer accompaniments of other conditions such as atherosclerosis senile ectasia trauma or bacterial endarteritis They are discussed further in Chapter 28 of this book

(b) *Aortic valve disease with regurgitation* is a much more common accompaniment of syphilitic aortitis than is aneurysm occurring in one quarter to one half of the cases diagnosed clinically though rarely early in the disease It was found in 36 5 per cent of the 126 cases of syphilitic aortitis examined post mortem by Clawson and Bell (1927) and in 27 per cent of the series of cases of cardiovascular syphilis of Moore and his associates (1932) which in turn made up 10 per cent of a clinical series of 6 420 patients with various forms of late syphilis It is due to a downward extension of the aortitis to involve primarily the commissures of the valve The inflammatory process widens the commissures and by separating the cusps produces regurgitation (Figure 131 shown on page 686) this is the reverse of the rheumatic effect which unites the cusps at the commissures to cause stenosis rather than regurgitation Extension of the syphilitic process may further damage the valve cusps themselves and cause their retraction or adhesion to the sinuses of Valsalva A very interesting finding is a rather rare eventration of one of the aortic valve cusps giving rise to a striking loud high pitched musical aortic diastolic murmur with thrill (Bellet et al 1939 Nichols 1940) A weakening of the aortic valve ring with stretching often comes with aortitis and is probably more commonly the cause of aortic regurgitation than is valve deformity per se Thus aortic regurgitation so frequently complicating syphilitic aortitis may result either from this stretching alone or from damage to the valve or from both factors The other heart valves are not affected by the syphilitic process directly except as the anterior cusp of the mitral valve may be somewhat involved or deformed by spread of the inflammatory

reaction down over it from the aortic valve or by retraction of the damaged aortic valve

(c) *Narrowing of the mouths of the branches of the thoracic aorta* by the inflammatory syphilitic process is an important and not infrequent complication of the aortitis It may even advance to the stage of actual occlusion *Coronary involvement of this nature* (Figure 89) *is particularly serious* and accounts in large part for the angina pectoris and especially for the sudden death so often occurring in patients with syphilitic aortitis It was found in 25 per cent of the series of 126 autopsied cases of syphilitic aortitis of Clawson and Bell (1927) and in over half (105 out of 199) of the autopsied cases of Venzoni (1939) Although the coronary arteries beyond their mouths are usually not involved in the process they may rarely be the seat of a syphilitic mesarteritis with narrowing and obstruction or even aneurysmal dilatation (Seydel 1935) Other arteries—the innominate carotid subclavian and intercostal—may also be more or less occluded at their mouths in syphilitic aortitis especially if there be in addition aneurysmal dilatation which compresses these arteries Such obstruction may lead to decrease and delay of one or both of the carotid or radial pulses and rarely to their obliteration with development of a collateral circulation to head or arms

Other arteries besides the aorta and coronary arteries may be attacked by the syphilitic process with thickening of wall thrombosis and occlusion or with stretching of the weakened wall and aneurysmal development There may be aneurysms anywhere in the body In themselves aneurysms exert little or no strain on the heart the strain comes if they perforate into veins (arteriovenous aneurysm) or if in the case of the aorta the coronary arteries are obstructed or the aortic valve is deformed Sclerosis of the pulmonary artery and its branches following syphilitic involvement of the bronchi and causing right ventricular failure and marked cyanosis (black cardiacs) was described in 1901 (Ayerza as quoted by Arrilaga in 1912—see bibliography of Chapter 20) but such a syphilitic sequela is excessively rare the great majority of cases of cor pulmonale with right heart failure and marked cyanosis are not syphilitic (see Chapter 20)

2 The second type of syphilitic involvement after that of the arteries is a *diffuse inflammatory reaction in the myocardium* with the presence of spirochetes (Warthin 1925 Magill 1935) Some cases of sudden death have shown this syphilitic myocarditis, but it is an infrequent manifestation of cardiovascular syphilis Rupture of a papillary muscle due to syphilitic myocarditis has been noted but it is exceedingly rare

3 The third type of cardiovascular syphilis is also rare and consists of the *invasion of the heart by gummata* These localized reactions to the presence of spirochetes may be situated anywhere in the heart—atrial walls ventricular walls or septum If they occur high in the interventricular septum they may involve the specialized conduction system of the heart—the atrioventricular bundle of His or its branches—and produce heart block of one type or another Gummata in the myocardium were found in only 3 of the 126

autopsied cases of Clawson and Bell s series (1927) Myxoid formations in the myocardium consisting of rounded translucid nodules have also been reported as a syphilitic lesion (Warthin 1916)

Symptoms Cardiovascular syphilis is often symptomless not only in its early stages but sometimes even when it has become far advanced It produces symptoms chiefly (1) by its involvement of the aortic valve which causes heart strain and eventual failure or (2) by its narrowing of the coronary artery mouths or walls to cause angina pectoris and even very rarely acute myocardial infarction (Burch and Winsor 1942) or (3) by the pressure of aneurysmal dilatation on surrounding tissue to cause pain or to obstruct blood flow in other vessels to block esophagus or air passages or to occasion hoarseness by involvement of the recurrent laryngeal nerve with paralysis The aortitis itself is almost always symptomless but sometimes a more or less constant dull ache high under the sternum has been ascribed to it even though there be no definite aneurysm

The earliest and commonest symptoms associated with cardiovascular syphilis which usually means aortitis are less commonly angina pectoris and more commonly paroxysmal dyspnea with or without cardiac asthma or frank pulmonary edema Either one or both may be present with no other symptoms at all or all the symptoms of congestive failure—more or less constant dyspnea weakness and pulmonary and systemic edema—may supervene to replace the angina pectoris or to appear at the very onset of evident trouble Sometimes pallor and loss of strength and weight also appear early in the disease

Sudden death is quite common in cardiovascular syphilis with or without preceding symptoms it was reported as having occurred in 39 of the 199 cases (20 per cent) in the series of Venzoni (1939)

Signs There may be no signs whatsoever of cardiovascular syphilis by any method of examination and the condition may be discovered only at postmortem examination Dilatation of the aorta which occurs after the process has advanced considerably may also escape attention for some time even after symptoms have appeared unless careful roentgenologic study is made Even when careful roentgenologic examination is carried out it is not possible to recognize early or slight syphilitic aortitis thereby for aortic dilatation and secondary calcification are after all rather late effects and actual dilatation of the first few centimeters of the aorta (a common site of syphilitic aortitis) may be present with no evidence by roentgen ray because the aortic shadow at its root is buried in that of the heart in all roentgenologic views and positions as carried out routinely However by the injection of a contrast medium such as Diodrast the root of the aorta can usually be delineated in doubtful cases

Later on when the process has become extensive and has advanced to the stage of aneurysmal formation of aortic regurgitation or of coronary obstruction ordinary methods of clinical examination may reveal it but by that time the situation may be hopeless Keen observation and careful study must

always be carried out when there is a suspicion of aortitis Since symptoms and signs often appear only when the disease is advanced however it will rarely be possible to pick up the early cases in spite of routine periodic examinations Routine examinations nevertheless especially of those individuals with a history of syphilitic infection, will sometimes reveal trouble that may be amenable to treatment before any symptoms have forced the patient to consult medical advice the value of these examinations should be universally realized

With aortitis alone or with aortic aneurysm without aortic regurgitation or coronary obstruction the heart remains normal in size without murmurs but when aortic valve disease develops with increasing regurgitation the heart enlarges rapidly and may eventually increase to enormous size to produce the typical *cor bovinum* With a considerable valve defect a loud aortic diastolic murmur develops louder than is found as a rule in rheumatic aortic valve disease and often heard best at the right of the upper sternum a moderate to loud aortic systolic murmur also is usually heard there (due to the aortic dilatation) the heart sounds are masked a functional mitral diastolic murmur (Austin Flint) is common and the peripheral pulse becomes water hammer in character along with the appearance of the so called capillary pulse Stenosis does not complicate the aortic regurgitation of syphilitic aortitis although aortic stenosis probably of rheumatic origin has been encountered along with syphilitic aortitis (for example three such cases noted by Cabot 1926) A curious loud high pitched musical character may be imparted to the aortic diastolic murmur with development of a palpable thrill when as already noted above there is an eventration of one of the valve cusps (Bellet et al 1939 Nichols 1940) It is to be remembered that the aortic regurgitation of syphilitic aortitis may begin gradually and at first may be but slight hence it is possible in some cases to find only a slight to moderate aortic diastolic murmur without a Corrigan pulse

There are three signs that have sometimes been adduced as evidence of early syphilitic aortitis before the development of aortic regurgitation or of well marked aortic dilatation they are (1) an aortic systolic murmur, (2) accentuation of or a tympanitic or metallic note to the aortic second sound and (3) *increased retrosternal percussion dullness These signs are all very* unreliable the first two being much more common in cases of aortic sclerosis with past or present hypertension and the third being found only when there is marked aortic dilatation or a widening of or disease in the mediastinum

The *serum reaction* for syphilis (Wassermann Kahn Hinton) is generally positive and strongly so in cardiovascular syphilis sometimes in approximately 15 per cent of the cases it is negative the Hinton reaction is more sensitive than the Wassermann test It must be remembered however that syphilis with a positive Wassermann reaction may be present as an incidental infection complicating chronic valvular disease or angina pectoris which is not of syphilitic origin this fact accounts I believe for a gross overestimation of

syphilitic aortitis as a cause of angina pectoris in some parts of the world in days gone by

The essential evidence of syphilitic aortitis is most commonly presented by roentgen ray examination the bulging of the thoracic aorta (especially the ascending portion and the arch) without other adequate reason (for example hypertension) affords the essential clue (Figure 146 page 770) The electrocardiogram remains normal until the heart enlarges as the result of aortic regurgitation with the development then of the pattern of left ventricular hypertrophy and dilatation (see Chapter 9) or until the coronary circulation is interfered with when one of the many patterns of coronary heart disease may appear

Course and prognosis The onset of cardiovascular syphilis is very slow and insidious When aortitis has becomes established years after the initial lesion and has come to light because of the symptoms or signs it has produced the course is often difficult and the prognosis is often poor Sometimes however treatment helps a good deal in relieving symptoms and in retarding the progress of the disease Spontaneous cures or rather cessation of symptoms without further development of signs are also seen Not infrequently in the course of a few months to several years after the discovery of the trouble death occurs suddenly with or without preceding angina pectoris or it may result from congestive heart failure some complicating infection or cerebral lesion or rarely rupture of an aneurysm Sometimes death comes quickly even in a few weeks sometimes it is postponed for ten to twenty or more years The average duration of life from diagnosis to death used to be about three years it has been increasing steadily since more effective therapy has been carried out One of the most important factors of all in controlling prognosis is the degree of physical activity of the patient the more strenuous the life in this respect the shorter it will be a relatively quiet existence undoubtedly prolonging life This fact is a prime reason for the very serious prognosis of cardiovascular syphilis among the Negro laborers Of 124 cases of syphilitic aortic regurgitation followed personally by Blackford 57 died within one year of the discovery of the lesion 27 more died during the next two years 17 were known to be alive after three years and 8 were still alive after five years (Blackford personal communication 1936) In all probability the factor of hard physical work is more important than that of race in this regard although it is true that the relative neglect of treatment may enter also

The effect of energetic specific treatment even of this late syphilis of aorta and heart on prognosis has been in the main distinctly favorably as has been demonstrated by a number of authorities (Moore et al 1932 Padget and Moore 1935 Buch 1945 Webster and Reader 1948) A study of 116 patients (103 men and 63 women) with late syphilitic cardiovascular lesions showed the following relative survival periods for well treated moderately treated and poorly treated cases 71 months 57 months and 16 months respectively (Buch 1945) Webster and Reader studied the microscopic

sections of the aortas of 45 patients with gross evidence of syphilitic aortitis at postmortem examination with relation to the effect of treatment The patients were divided into untreated inadequately treated and adequately treated groups the criterion of adequate treatment being a minimum of at least 20 arsenical and 20 bismuth injections, only three of 19 patients adequately treated showed any activity of the process while all 9 untreated cases showed active cellular infiltration of the aorta

Sudden death *is occasionally the result of an undiagnosed syphilitic involvement* of aorta or heart without previous symptoms or signs The medical examiner or coroner establishes the cause of death If such cases were added to those in whom the diagnosis has been made before death the statistics of the total number of cases of cardiovascular syphilis in the community would be slightly increased but probably by not more than a very few per cent at most depending of course on the thoroughness of medical examination and care and of postmortem examinations in that particular community

The prognosis may be made worse in rare cases by too vigorous therapy Heart failure and even death have followed directly in a few cases from overzealous efforts to cure

Complications The important complications of cardiovascular syphilis have already been referred to under the heading of pathology—aneurysms angina pectoris coronary occlusion (not coronary thrombosis) and congestive heart failure Other types of heart disease or of vascular disease may be present in particular arteriosclerosis of aorta or of coronary arteries chronic rheumatic valvular disease hypertension and uncommonly subacute bacterial endocarditis A confusing picture is sometimes presented by the aorta when syphilis and atheroma are present together this not infrequently happens in older patients Syphilitic aortitis predisposes to sclerosis elongation and tortuosity of the aorta but apparently not much to dissecting aneurysms Pericarditis is a rare complication of aortitis and is not a part of the syphilitic picture Important cardiac arrhythmias are also uncommon especially atrial fibrillation Premature beats are occasionally seen and are frequently followed by pulsus alternans if the left ventricle is weak Heart block *either atrioventricular or intraventricular in type is found now and then but it is rarely* of high grade complete atrioventricular block and bundle branch block *are much more commonly* the result of nonsyphilitic coronary disease

Central nervous system syphilis complicates cardiovascular syphilis in from 20 to 30 per cent of the cases while cardiovascular syphilis has been reported in 20 to 25 per cent of cases of general paresis and in from 15 to 50 per cent of cases of tabes dorsalis

Treatment With the advent of penicillin the discussion of the treatment of cardiovascular syphilis needs radical revision It resembles that of subacute bacterial endocarditis in that a really specific and curative therapy of the active disease process has been introduced though leaving behind it as in the case of subacute bacterial endocarditis too a scarred heart but it differed markedly in the past in that there already existed for cardiovascular syphilis

reasonably good therapy Although penicillin may eventually completely replace the heavy metals namely arsenic bismuth and mercury in the treatment both of syphilis initially and of its sequel of cardiovascular disease I shall retain here for use even if only supplementary and for historic interest during transition much of the detail of the therapy presented in the last edition of this book

Current experience has established the value and safety of penicillin therapy of cardiovascular syphilis and therefore such treatment is more and more replacing that with the heavy metals At first it was feared that the speedy resolution of the active disease in aorta and heart might have serious consequences in the way of weakening the wall and of inducing the Jarisch Herxheimer reaction Hence at first very small doses of penicillin were administered for example, 500 to 3 000 units but as time went on it was discovered that much larger amounts could be safely and effectively given 25 000 to 100 000 units (Tucker and Farmer 1947 Moore et al 1948 Kossmann and Flaum 1948 Porter 1948) But apparently the coexistence of neurosyphilis especially general paresis does increase the threat of the Herxheimer reaction (Moore et al 1948) Several authorities have recommended for the adequate treatment of cardiovascular syphilis a total dosage of from 5 000 000 to 15 000 000 units of sodium penicillin given in aqueous solution by intramuscular injection over a period of about three weeks for example 40 000 units every three hours for 150 doses (Kossmann and Flaum 1948) Procaine penicillin in the dosage of 600 000 units once daily in the buttocks or 300 000 units twice daily for ten days to two weeks can be more conveniently administered

For particular symptoms special treatment is indicated as in the use of the nitrites for angina pectoris or digitalis and if necessary diuretics for congestive failure and of hypnotics and narcotics for insomnia and aneurysmal pressure pains For intractable angina pectoris and pains due to pressure or erosion by an aneurysm paravertebral sympathectomy or alcohol injection has proved of much value (see Chapter 21) Total thyroidectomy is contraindicated

It is regarding specific antisyphilitic therapy with the heavy metals that there was much disagreement in the past Some were for forcing it vigorously in the hope of stopping the progress of the disease others would give none for fear of weakening the aortic wall or myocardium by too rapid a destruction of treponemata and resolution of inflammatory tissue with resultant heart failure or increased stretching of aortic wall The wisest course undoubtedly rested between these two extremes—namely the careful long-continued administration of a moderate amount of antisyphilitic drugs determined in each individual case by the condition and needs of that case In the presence of congestive failure antisyphilitic therapy was withheld until treatment of the failure had been successful but today penicillin can be given concurrently under careful supervision

The technic in the use of the heavy metals which has been successful in

many cases of cardiovascular syphilis in the past may best be quoted directly from the several paragraphs concerned in the last edition (1944) of this book The only debatable point concerns the addition of potassium iodide which although traditional has been omitted by a number of authorities without detracting from the success of the treatment Incidentally it has not been necessary to add potassium iodide to penicillin in the new therapy of syphilis It seems reasonable therefore to place in brackets the reference to potassium iodide in the quoted paragraphs

The following procedures for the administration of specific therapy in cardiovascular syphilis although by no means the only methods that may be employed have proved by extensive experience to be satisfactory If the diagnosis is certain or reasonably sure and congestive failure or serious renal and hepatic disease are not present therapy is begun with mercury or preferably bismuth and potassium iodide It is preferable to begin with bismuth in the form of an insoluble salt (the subsalicylate) by intramuscular injection in the dosage of 0 1 gram (1½ grains) every four days for four weeks and then 0 2 gram (3 grains) weekly for another eight weeks [Simultaneously with the bismuth potassium iodide should be given by mouth 2 0 to 3 0 grams (30 to 45 grains) three times daily] Th drugs must be decreased in dosage or stopped if toxic symptoms arise such toxic symptoms consist chiefly of salivation in the case of bismuth [and of urticaria, erythema lachrymation and coryza in the case of potassium iodide] Also there must be a pause in the specific antisyphilitic therapy if congestive heart failure supervenes except that either of the two excellent mercury diuretics Salyrgan (Mersalyl) or Mercupurin (Novurit) may be injected intravenously or intramuscularly in the dosage of 2 cc weekly or once every few days until the congestion is cleared up such therapy acts however in combating the heart failure rather than in controlling the cardiovascular syphilis

At the end of this first course of twelve weeks arsenic should be cautiously added to the therapy if the condition of the patient warrants as it usually does Mapharsen in twelve weekly intravenous injections beginning with 0 02 gram and increasing gradually to a maximum dose of 0 04 gram is desirable if possible Bismarsen (bismuth arsphenamine sulphonate) may be given instead of Mapharsen to the less favorable that is the sicker patients by intramuscular injection of 0 1 gram every five days increasing to 0 2 gram at a dose for a period of twelve weeks

At the end of this second course one should return without pause to the therapy used in the first course injections of an insoluble bismuth salt [along with potassium iodide] These two courses should then be alternated every three months for a minimum period of two years After that one course of bismuth followed by one course of Mapharsen or Bismarsen should be given annually for the duration of the patient s life

Such antisyphilitic therapy as has been outlined above may now and then yield striking results with decrease or disappearance of angina pectoris or of heart block or with cessation of growth or even decrease in size of aorta or aneurysm In many cases it merely retards the progress of the disease Rarely it does harm but discrimination in the selection and administration of the therapy obviates almost all danger Taking everything into consideration prolonged but not rapid specific

therapy of cardiovascular syphilis is well worth while Not only is life prolonged by adequate therapy (by several years in Moore s series of cases of aortic aneurysm and syphilitic aortic regurgitation as compared with control cases—Moore et al 1932 and Padget and Moore 1935) but symptoms are decreased and disability is lessened

The most important consideration of all however with respect to cardio vascular syphilis is that it is a preventable disease early and thorough treatment of the initial syphilitic infection should practically wipe out syphilitic aortitis and its sequelæ

Differential diagnosis Cardiovascular syphilis chiefly in the form of aortitis is to be differentiated particularly from angina pectoris of nonsyphilitic origin from chronic valvular disease of rheumatic nature especially affecting the aortic valve from a kinked or tortuous aorta due to extensive atherosclerosis or to a high position of the diaphragm with horizontally placed heart simulating a dilated aorta in the roentgenologic anteroposterior view but easily identi fied in the oblique views from mediastinal tumors which may simulate aortic dilatation or aneurysm by physical examination and roentgen ray and from hypertensive arteriosclerotic heart disease with aortic dilatation aortic regurgitation and congestive failure Very rarely there may exist acute gumma tous myocarditis simulating acute myocardial infarction (Reifenstein 1936) All signs and symptoms including the Wassermann and Hinton reactions must often be considered together before a definite diagnosis can be arrived at sometimes even then it is impossible to differentiate syphilitic aortitis from these other conditions The only fairly certain sign is that of the presence of an aneurysm of the thoracic aorta in the male aneurysms of the abdominal aorta are generally arteriosclerotic as are also rare thoracic aneurysms in old women The earliest stage of aortitis cannot be diagnosed clinically the aorta being at that time of normal size and shape

Aortic syphilis has been and in fact is still being overdiagnosed in the presence of the combination of angina pectoris or aortic regurgitation and of a positive serologic reaction or a history of syphilitic infection In truth angina pectoris is uncommonly due to syphilis even though syphilis is present in the case and also in some parts of the world where rheumatic heart disease is common rheumatic aortic regurgitation and syphilis with or without aortitis may be present in the same patient

BIBLIOGRAPHY

CARDIOVASCULAR SYPHILIS

Beckh W The Serologic Reaction in Cardiovascular Syphilis *Am Heart J* 1943 XXV 307

Bell E T Frequency with Which Syphilitic Lesions are Encountered in Postmortem Examinations" *Arch Path* 1938 XXVI 839

Bellet, S et al "Loud Musical Diastolic Murmurs of Aortic Insufficiency" *Am Heart J* 1939 XVIII 483

Blackford L M Syphilitic Aortic Insufficiency Cases of Unusual Duration" *J M A Georgia* 1935 XXIV No 9

Burch G E and Winsor T Syphilitic Coronary Stenosis with Myocardial Infarction *Am Heart J* 1942 XXIV 740

Cabot R C 'The Four Common Types of Heart Disease An Analysis of Six Hundred Cases *J A M A* 1914 LXIII 1461

Facts on the Heart W B Saunders Co Philadelphia 1926

Clawson B J Syphilitic Heart Disease" *Urol & Cutan Rev* 1941 XLV 219

Clawson B J and Bell E T "The Heart in Syphilitic Aortitis" *Arch Path and Lab Med* 1927 IV 922

Evans B Syphilitic Thoracic Aneurysm in Young Adults *Brit M J* 1941 I 851

Gelperin A The Incidence of Syphilitic Aortitis in a Representative Municipal Hospital *Am Heart J* 1940 XX 340

Lancisi J M *De novissime observatis abscessibus* Rome 1724

McCulloch H Congenital Syphilis as a Cause of Heart Disease *Am Heart J* 1930, VI 136

Magill T P Syphilitic Myocarditis" *Bull Johns Hopkins Hosp* 1935 LVII 27

Maynard E P Jr 'The Present Status of the Diagnosis of Uncomplicated Syphilitic Aortitis *Bull New York Acad Med* 1942 XVIII 383

Moore J E Danglade J H and Reisinger J C Diagnosis of Syphilitic Aortitis Uncomplicated by Aortic Regurgitation or Aneurysm Comparison of Clinical and Necropsy Observations in One Hundred and Five Patients *Arch Int Med* 1932, XLIX 753

Treatment of Cardiovascular Syphilis Results Obtained in Fifty three Patients with Aortic Aneurysm and in One Hundred and Twelve with Aortic Regurgitation. *Ibid* 1932 XLIX 879

Morgagni G B *De Sedibus et Causis Morborum* Ex typog Remondiniana Venice 1761

Nichols C F A Study of Syphilis of the Aorta and Aortic Valve Area" *Ann Int Med* 1940 XIV 960

Norris R F Syphilitic Aortitis in Childhood and Youth Report of Two Cases with Sudden Death *Bull Johns Hopkins Hosp* 1935 LVII 206

Padget P and Moore J E 'The Results of Treatment in Cardiovascular Syphilis A Report of Three Years Additional Observation *Am Heart J* 1935 X 1017

Pare A *Opera Chirurgica* Apud J Fischerum Francofurti and Moenum 1612 (French translation Paris 1840 Vol 1 p 372) (1st French ed 1664)

Reifenstein E C Acute Gummatous Myocarditis Simulating Acute Myocardial Infarction *Ann Int Med* 1936 X 241

Reuter K "Ueber Spirochaete pallida in der Aortenwand bei Hellerscher Aortitis *Munch med Wchnschr* 1906 LIII 778

Seydel F C "Uber die luetische Erkrankung der Herzkrankgefasse mit einem Fall eines syphilitischen Aneurysmas an dem vorderen absteigenden Ast der linken Kranzarterie *Ztschr f Kreislauff* 1935 XXXVII 265

Stadler E *Syphilis des Herzens und der Gefasse* Theodor Steinkopff Dresden and Leipzig 1932

Stone C T and Vanzant F R Heart Disease as Seen in a Southern Clinic A Clinical Pathological Survey" *J A M A* 1927 LXXXIX 1473

Venzoni M "La sifilide dell apparato circulatorio dal punta di vista anatomopathologico *Arch Ital d anat e istol pat* 1939 X 171

Warthin A S Myxoma like Growths in the Heart Due to Localization of Spirochaeta Pallida" *J Infect Dis* 1916 XIX 138

"Sudden Death Due to Exacerbation of Latent Syphilitic Myocarditis" *Am Heart J* 1925 I 1

Welty J W "Necropsy Survey of Cardiovascular Syphilis with Particular Reference to Its Decreasing Incidence" *Am J M Sc* 1939 CXCVII 782

White P D Chamberlain F L and Kelson S R "Rupture of Aorta into Pulmonary Artery with Long Survival" *Ann Int Med* 1941 XV 589

White P D and Jones T D "Heart Disease and Disorders in New England" *Am Heart J* 19 8 III 302

White P D and Wise N B "The Early Diagnosis of Cardiovascular Syphilis" *New England J Med* 1937 CCXVII 988
Williams A W Heart Disease in the Native Population of Uganda " *East African M J* 1938 XV 279
Wright, J H and Richardson O "Treponemata (Spirochaetae) in Syphilitic Aortitis. Five Cases One with Aneurism *Boston M and S J* 1909 CLX, 539

Recent References (1944–1950)

Buch H. "Prognosis of Late Syphilitic Cardiovascular Lesions *Acta med Scandinav* 1945 CXXII 529
Clawson B J "Syphilitic Cardiac Deaths in over Fifty Thousand Autopsies *Minnesota Med.*, 1950 XXXIII 437
Edeiken, J Ford, W T Falk M S and Stokes J H Penicillin Treatment of Patients with Cardiovascular Syphilis in Congestive Failure *Circulation* 1950 I 1355
Elkeles A Calcification of Ascending Aorta as a Diagnostic Sign of Syphilitic Aortitis " *Proc Roy Soc Med* 1949 XLII 867
Goldstein P "Spontaneous Rupture of Syphilitic Saccular Aneurysms of the Ascending Aorta into the Pericardial Cavity with Hemopericardium Report of Sudden Death in Twenty nine Cases " *Arch Int Med* 1949 LXXXIV 540
Kossmann C E., and Flaum G Penicillin in the Treatment of Cardiovascular Syphilis " *Mod Concepts Cardiovas Dis* 1948 XVII No 1
Moore J E "Cardiovascular Syphilis Summary of Recent Information with Special Reference to Treatment with Penicillin" *Am J Syph* 1949 XXXIII 43
Moore J E Farmer T W and Hoekenga M T "Penicillin and the Jarisch Herxheimer Reaction in Early Cardiovascular and Neurosyphilis " *Tr A Am Physicians* 1948 LXI 176
Peabody G E Reader G G Dotter C T and others Angiocardiography in Diagnosis of Cardiovascular Syphilis " *Am J M Sc* 1950 CCXIX, 242
Porter R R "Penicillin in Cardiovascular Syphilis *Virginia M Monthly* 1948 LXXV 357
Scharfman W B Wallach J B and Angrist A Myocardial Infarction due to Syphilitic Coronary Ostial Stenosis *Am Heart J* 1950 XL 603
Thorner M C Carter R A and Griffith G C Calcification as a Diagnostic Sign of Syphilitic Aortitis " *Am Heart J* 1949 XXXVIII 641
Tucker H A and Farmer T W Penicillin in Cardiovascular Syphilis Early Reactions to Administration " *Arch Int Med* 1947 LXXX 322
Webster B and Reader G G "The Effect of Antisyphilitic Treatment on the Microscop Appearance of Syphilitic Aortitis " *Am J Syph* 1948 XXXII 19
White P D "The Relative Incidence of the Etiologi Types of Heart Disease in New England Compared to That of 25 Years Ago An Analysis of 3000 Cases In press 1951

CHAPTER 17

THE HEART IN DIPHTHERIA, SCARLET FEVER, AND TUBERCULOSIS AND IN OTHER BACTERIAL INFECTIONS, INFESTATIONS, AND VIRUS DISEASES

Although this chapter is steadily shrinking in importance in the overall picture of cardiovascular disease because of current improvement in the control of infectious diseases both prophylactically and therapeutically throughout the world our knowledge of the cardiovascular effects of many diseases has widened and deepened during the last generation as in the case of the virus diseases

Two or three generations ago the bulk of all heart disease was blamed on infections many cases were rightly so labeled but many more were incorrectly diagnosed particularly those with unrecognized congenital hypertensive and coronary heart disease Now infectious cardiovascular defects are known to comprise but a minority of all cases of clinical heart disease one reason for this change in viewpoint is the actual decrease in certain serious infections that can cause primary damage to the circulation but the more significant reason is the correction of the old time exaggerated point of view It is true however that many diseases which may be fatal show changes in the heart that are terminal in nature though not present in serious degree during life and that even the infections which do not directly cause heart disease can be serious or fatal complications in cardiac cases so that their control does have an important effect on the longevity of persons with heart disease An interesting comparison of the standardized death rates per 100 000 among insured persons aged 1 to 74 years in this country in the years 1917 1941 and 1948 has recently been made possible (*Statistical Bulletin* Metropolitan Life Insurance Company March 1942 Vol 23 No 3 Dublin personal communication 1949) diphtheria in 1917 showed a rate of 21 7 in 1941 only 0 7 and 0 4 in 1948 syphilis 19 1 in 1917 9 1 in 1941 and 4 8 in 1948 pneumonia (all forms) 131 8 in 1917 23 0 in 1941 and 15 2 in 1948 typhoid

fever 12 0 in 1917 0 8 in 1941, and 0 1 in 1948 and tuberculosis (all forms) 202 2 in 1917, 40 9 in 1941 and 25 9 in 1948

Having considered in the last three chapters the more important cardiovascular infections, rheumatic acute and subacute bacterial and syphilitic we turn now to other infections which have a relatively uncommon or unimportant effect on the heart Only occasionally do a few of these infections cause serious heart disease

DIPHTHERIA

Diphtheria during and following World War II has had a recrudescence of importance because of its increased frequency in the wake of the hardships in Europe and Asia and of its protean form among the military forces of the U S A It often causes important damage to the heart muscle but happily it has been robbed of so much of its threat in recent years by large scale prevention of the disease in the first place and secondly when it does occur by the use of antitoxin that much less diphtheritic heart disease is nowadays diagnosed than was the rule a generation ago During World War II nonfaucial diphtheria was on occasion unrecognized when it attacked other parts of the body especially the skin and serious cardiac effects were at times noted before a correct diagnosis was made

Pathology The acute effect of severe diphtheria which is not quickly or sufficiently combated by antitoxin may be serious There is clear evidence that grave myocardial damage may occur and that this may lead to death The diphtheria bacillus itself is rarely encountered in the heart it acts evidently through the toxin it produces which circulating in the blood stream reaches the heart muscle The necrosis (Figure 90) produced in the myocardium may be found only at postmortem examination or it may give evidence during life by the production of various grades of atrioventricular or intraventricular block (shown by electrocardiogram) or rarely of heart failure In some cases there may be multiple small hemorrhages throughout the heart as well as in other parts of the body (as in the liver and intestines) and it seems likely that such hemorrhages in the heart muscle may play some role in the sickest cases Undoubtedly death during diphtheria results from the myocardial involvement in a considerable percentage of the fatal cases such death may come abruptly without warning or after giving evidence such as that noted above Endocarditis and pericarditis are not caused by diphtheria, except in unique cases (Sutherland and Willis 1936)

There is very infrequently any clinical evidence of a chronic effect on the heart from diphtheria even when it has been severe Survival usually means escape from any permanent or serious heart disease Slight lesions which may be discovered by microscopic examination of the myocardium doubtless occur in some cases but they are not demonstrable by clinical examination Therefore it is reasonable to infer that any serious sequelae are absent rather than present. Rare cases of chronic atrioventricular or intraventricular heart block

CHAPTER 17

THE HEART IN DIPHTHERIA, SCARLET FEVER, AND TUBERCULOSIS AND IN OTHER BACTERIAL INFECTIONS, INFESTATIONS, AND VIRUS DISEASES

Although this chapter is steadily shrinking in importance in the overall picture of cardiovascular disease because of current improvement in the control of infectious diseases both prophylactically and therapeutically throughout the world our knowledge of the cardiovascular effects of many diseases has widened and deepened during the last generation as in the case of the virus diseases

Two or three generations ago the bulk of all heart disease was blamed on infections many cases were rightly so labeled but many more were incorrectly diagnosed particularly those with unrecognized congenital hypertensive and coronary heart disease Now infectious cardiovascular defects are known to comprise but a minority of all cases of clinical heart disease one reason for this change in viewpoint is the actual decrease in certain serious infections that can cause primary damage to the circulation but the more significant reason is the correction of the old time exaggerated point of view It is true however that many diseases which may be fatal show changes in the heart that are terminal in nature though not present in serious degree during life and that even the infections which do not directly cause heart disease can be serious or fatal complications in cardiac cases so that their control does have an important effect on the longevity of persons with heart disease An interesting comparison of the standardized death rates per 100 000 among insured persons aged 1 to 74 years in this country in the years 1917 1941, and 1948 has recently been made possible (*Statistical Bulletin* Metropolitan Life Insurance Company March 1942 Vol 23 No 3 Dublin personal communication, 1949) diphtheria in 1917 showed a rate of 21 7, in 1941 only 0 7 and 0 4 in 1948 syphilis 19 1 in 1917 9 1 in 1941 and 4 8 in 1948 pneumonia (all forms) 131 8 in 1917 23 0 in 1941 and 15 2 in 1948 typhoid

but weakness and listlessness are the commonest symptoms accompanying the cardiac involvement and these may be due rather to the general effect of diphtheria on the whole body (nervous system vasomotor control and musculature) than to the cardiac involvement With the rare complication of congestive heart failure cough may appear

Signs Signs also are relatively infrequent There may appear pallor cyanosis cardiac enlargement due to dilatation tachycardia diastolic gallop rhythm (which may be due either to delayed atrioventricular conduction or to cardiac dilatation and failure or to both) an apical systolic murmur due to secondary mitral regurgitation or an arrhythmia which may include an ominous ventricular paroxysmal tachycardia and rarely bradycardia due to heart block There may be hepatic engorgement and tenderness and pulmonary rales due to heart failure If a majority of these signs are present the immediate prognosis is very serious

Fever is not a sign of diphtheritic myocardial involvement in fact the most serious heart trouble exists after the fever of the acute illness is over Fluoroscopic examination if such can be safely undertaken may show dilatation of the heart Electrocardiographic examination is of greater value than any other special method by revealing the degree of atrioventricular or intraventricular (bundle branch) block or more commonly abnormalities of the *T* wave Blood and urine examinations and other such studies are not of much help

Course and prognosis When involvement of the heart in diphtheria reveals itself by signs or symptoms the course of the illness is short and fatal or long and exhausting with the prognosis in doubt Although about half of such cases recover they are not out of danger for weeks and they may die suddenly at any time during this period of convalescence Heart block is usually a fatal sign especially bundle branch block A follow up study of cases of diphtheria at the South Department of the Boston City Hospital has revealed a few survivors after the development of atrioventricular or intraventricular block On recovery from the diphtheria such cases have lost all electrocardiographic evidence of heart block except for very rare individuals who retained some degree of atrioventricular block there were none in this particular series in whom intraventricular (bundle branch) block persisted (Faulkner and Place personal communication) though one such case was reported by Perry (1939) *T* wave changes also tend to clear up although rarely inversion of this wave in Lead 1 or Lead 2 has persisted for a few months or even a few years

Complications Heart block and cardiac dilatation have been mentioned as grave cardiovascular complications of diphtheria There are two other serious cardiovascular complications difficult to analyze namely vagal and splanchnic paralyses The tachycardia in diphtheria has sometimes been ascribed to vagal paralysis resulting from damage to this nerve by the diphtheritic toxin and also to circulatory failure from vasomotor (splanchnic) paralysis the latter has also been blamed for some of th[illegible]

probable that these are real factors how responsible they may be as pared to actual myocarditis we do not know, it is probable that all factors operate simultaneously in a seriously sick patient

Treatment In the first place adequate antitoxin should be given at the of the diphtheria, the more severe the illness the more units of antitoxin sl be administered even up to 50,000 or 100 000 This early therapy is the important of all measures to protect the heart Rest in bed should b forced for at least several days after all signs of infection have gone ev the mildest cases and for several weeks in the severe cases especially if have been symptoms or signs of cardiac involvement For serious cardiovas complications absolute rest and intravenous dextrose (glucose) injec (25 to 100 cc of 50 per cent solution daily or oftener) have been found helpful than other measures Digitalis, epinephrine (adrenaline) and stimulating drugs with the possible exception of caffeine and theoph ethylene diamine (aminophyllin), have been disappointingly ineffecti the treatment of cardiac failure and vasomotor collapse in diphtheria adequate treatment of the infection itself will prevent such complications

Differential diagnosis The differential diagnosis of diphtheritic heart di is usually not difficult It must be distinguished from the unimportant n circulatory asthenia (effort syndrome) that may come in diphtheria as in infectious disease from the tachycardia due to vagal paralysis and from cident heart disease such as rheumatic valvular disease It must be born mind also that diphtheria of the skin or mucous membranes other tha the fauces can result in serious heart disease

SCARLET FEVER

There is strictly speaking probably no such entity as the scarlet f heart although there may occasionally occur temporary toxic cardiac ef Permanent heart disease certainly does however follow scarlet fever in ra rare cases Evidence that has been accumulating in the past few years indic that scarlet fever like certain other streptococcus infections merely plays role of an activating agent of the rheumatic infection in the heart in viduals who belong to rheumatic families (Paul Salinger and Zuger 19 Faulkner Place and Ohler 1935) Further important evidence that sc fever per se does not cause any important myocardial disease has been vanced by Shookhoff and Taran (1931) who found in the electrocardiogr of fifty consecutive patients with scarlet fever only minor changes in th waves or *Q T* intervals in 10 per cent and no prolongation of the *P R* inte in any case in contrast to the frequent changes especially prolongation of *P R* interval in acute rheumatic heart disease The statistical evidence wh we possess at present indicates that not over 0 5 per cent of all cases scarlet fever are complicated by endocarditis or pericarditis or both and a very small fraction of 1 per cent of cases of heart disease originate du scarlet fever The chronic valvular disease that results is of rheumatic ty

but it does not ordinarily develop to the stage of marked valve deformity The mitral is the valve ordinarily attacked the aortic rarely In a series of 602 cases of scarlet fever observed during one year (August 1943 to August 1944) 36 (6 per cent) showed cardiac complications during the acute illness 32 with myocarditis of whom one died with atrial fibrillation and two others showed partial a v block and 4 with endocarditis (Neubauer 1945)

It is especially in patients in whom acute polyarthritis complicates scarlet fever that acute cardiac infection tends to occur valvular disease has how ever also been reported in scarlet fever with no arthritis It is important always to wait until the completion of convalescence before ascribing to valvular damage an apical systolic murmur which may be merely a temporary accom paniment of the scarlet fever itself More than half of the cases of acute endocarditis or pericarditis occurring in scarlet fever show an arthritis at the onset of the heart disease

The pathologic changes are similar to those of rheumatic heart disease both in the acute and in the chronic stages

There are no symptoms of the heart involvement itself except for a slight prolongation of the fever and occasionally pain from pericarditis

The only signs are the development of slight cardiac enlargement and of heart murmurs rarely the occurrence of a pericardial friction rub during or at the end of the scarlet fever and minor electrocardiographic changes noted above

The treatment of scarlet fever and therefore favoring the prevention of the infrequent heart disease that results has been improved since the introduc tion of penicillin which should be administered at the very onset of the hemolytic streptococcus sore throat which ushers in the scarlet fever and continued until convalescence begins in order to prevent especially the formerly serious and common complication of mastoiditis

The differential diagnosis is inconsequent in that the acute heart disease with or without pericarditis occurring during scarlet fever and the chronic valvular disease that may follow are indis inguishable from rheumatic heart disease acute and chronic

STREPTOCOCCUS HEMOLYTICUS INFECTION WITH HEMORRHAGIC NEPHRITIS

Among others Whitehill Loncope and Williams (1939) have called atten tion to this serious disease in childhood which is not infrequently attended by a complication of cardiac dilatation and even heart failure early in the illness (71 per cent of the series of 138 cases of Whitehill et al) but fortunately nowadays penicillin given as near the onset of the disease as possible can result in much improvement and may help to prevent the more serious cardiac effects provided the streptococcus infection itself is still active the penicillin does not cure the nephritis itself The death rate used to be fairly high (20 3 per cent of the 59 severe cases in the series just mentioned) recovery was

slow but the heart did often return to normal (see also Chapter 23) Happily the picture has changed and this disease should be on the way out

PNEUMONIA

Pneumonia either lobar or bronchial in type may prove a great strain for an already weakened or diseased heart but it does not itself cause serious heart disease except in rare instances when acute bacterial (generally pneumococcus) endocarditis or a septic pericarditis occurs in either case almost always a fatal complication in the days before chemotherapy with the sulfonamide drugs and the introduction of the antibiotics especially penicillin but this complication is now largely preventable and most cases that do occur are curable by the use of these drugs (formerly sulfadiazine sulfathiazole or sulfapyridine 1 to 2 gm 15 to 30 gr 3 or 4 times a day for a few days under careful observation and with blood titration and now preferably procaine penicillin by intramuscular injection 300 000 units daily for a few days to a week or terramycin chloromycetin, or aureomycin by mouth about 500 mg every 6 hours for a week) The various antibiotics should be appraised as to their efficacy by direct testing on the growth of the responsible organisms themselves

Electrocardiograms in the course of and immediately following severe pneumonia may show various arrhythmias and sometimes important changes such as inversion of the *T* waves and prolongation of the *P R* interval the more severe the disease the more marked the changes but these abnormalities subside during convalescence Undoubtedly they are to be ascribed to a direct toxic effect on the myocardium (Cohn and Jamieson 1917 Master et al 1931) At postmortem examination the heart muscle cells may show cloudy swelling but such a finding does not constitute real heart disease

As will be observed concerning typhoid fever and exanthematic typhus the weakness and collapse due to pneumonia are not the result of cardiac failure but of the infection It is therefore not to be expected that routine digitalis therapy in pneumonia should help except when there is obvious congestive failure or a rare complication such as atrial fibrillation or atrial flutter

TYPHOID FEVER

The rare invasion of the endocardium by the typhoid bacillus producing acute or subacute bacterial endocarditis has already been mentioned (Chapter 15) Much more common but of little or no clinical importance is the finding at postmortem examination of slight to moderate scattered toxic changes of muscle fibers and interstitial tissue consisting of cloudy swelling and infiltration with small round cells in the majority of cases dying of typhoid fever Also periarteritis and endarteritis have been found in the blood vessels of such patients even to the extent of causing ulceration and aneurysm of the aorta Pericarditis is a rare complication

Generally the heart is not affected to any important or appreciable degree

in typhoid fever Not infrequently, however *T* wave changes (flattening or inversion) and rarely delayed atrioventricular conduction can be found by electrocardiogram during the acute infection but no high degree of block (Brow 1929 Porter and Bloom 1935 Mainzer 1947) and if cardiovascular symptoms occur they are in the nature of the effort syndrome usually found in infectious disease Of course organic heart disease of other nature may happen to complicate and be overburdened by the infection but it is wrong to treat the heart with digitalis or other such drug in order to combat the symptoms of effort syndrome or of circulatory failure due to vasomotor paresis It is apparently not heart failure that kills in typhoid fever but the toxic effect with weakness and vascular collapse resulting from the infection Also avitaminosis associated with the malnutrition during a prolonged illness with typhoid fever may play a role electrocardiographically and otherwise (Rachmilewitz and Braun 1948)

TUBERCULOSIS

Tuberculosis does not cause heart disease itself except in rare cases in which there is direct tuberculous invasion of the myocardium or endocardium Pericardial tuberculosis is however occasionally encountered as either (1) an isolated lesion (2) a part of a polyserositis or (3) an extension from mediastinal tuberculosis

Tuberculosis of the myocardium is infrequently found at postmortem examination as a part of a miliary tuberculous process or in the form of a solitary tubercle or abscess It is an autopsy finding rarely even suspected during life The miliary tubercles in the heart muscle almost never produce any symptoms or signs the illness being that usually observed in miliary tuberculosis If invasion or pressure directly involves the atrioventricular conduction system heart block may occur with arrhythmia and slow pulse or myocardial tuberculosis may even cause congestive heart failure (Wilbur 1938 also personal observation 1947) Still more rare than disease of the heart muscle in miliary tuberculosis is a myocardial invasion by a solitary tubercle or tuberculous (cold) abscess such invasion is usually symptomless and without signs but it is capable of causing an aneurysm of the heart wall which may even lead to rupture and to death In a series of 7 683 cases of tuberculosis myocardial tuberculosis was found 49 times (0 63 per cent) (Raviart 1906)

Tuberculous endocarditis is also rare infrequent cases usually of miliary tuberculosis revealing at autopsy tubercles in the endocardium of the heart walls and of the valves or tuberculous ulceration of the endocardium Tubercle bacilli have been found in such endocardial lesions There is no evidence that chronic valvular disease can originate either directly from tuberculous inflammation or indirectly from the toxic effect of tuberculosis elsewhere in the body

Tuberculous pericarditis is not rare It is an important type of acute and also of chronic pericardial disease isolated or more commonly associated

with a similar involvement of pleura or with a tuberculous involvement of the mediastinum arising from lymphatic glands, spinal caries, or other cause It is not usually accompanied by myocardial or endocardial tuberculosis but in rare cases for example in miliary tuberculosis it may be thus complicated Isolated tuberculosis of the pericardium unsuspected during life has been discovered to be an occasional cause of death in elderly individuals (Thompson 1933)

Pericardial effusion is a common accompaniment of pericardial tuberculosis and may be very slow and insidious in its onset causing few or no symptoms at first but finally incapacitating the patient by its pressure effect, which prevents adequate filling of the heart (cardiac tamponade—see Chapter 27) or by associated fever and weakness The effusion often in fact usually hemorrhagic in character may develop to enormous size (even up to 2 or 3 liters) and because of its very gradual growth may be astonishingly well supported for a long time even for many weeks it is much better endured by the patient than is the more acute rheumatic pericardial effusion of the same amount of fluid The tuberculous effusion may be spontaneously absorbed or with the development of serious symptoms and signs require paracentesis The symptoms—dyspnea cough and oppression—come from pressure effects and but rarely include sharp pains such as are frequent in rheumatic pericarditis The signs are those of a small moderate or large accumulation of fluid in the pericardium with slight moderate or enormous increase of the area of percussion dullness over the heart and of the roentgen ray shadow With a large effusion the arterial blood pressure is low especially the pulse pressure, there is often a well marked paradoxical pulse and the systemic venous pressure is elevated with resulting prominence of the jugular veins and pulse and enlargement of the liver these are signs of acute or subacute constrictive pericarditis (the so called cardiac tamponade) A pericardial friction rub may be heard over the precordium even in the presence of a large effusion

After the subsidence of the acute process a serious chronic pericarditis may develop frequently with involvement of the mediastinum If extensive this chronic mediastinopericarditis may so cramp the heart chambers and great veins that the entrance of blood into the heart is obstructed Generally the obstruction is most manifest in the hepatic veins with resulting hepatic engorgement and ascites this condition has therefore been called chronic mediastinopericarditic pseudocirrhosis of the liver or Pick s disease (Chevers 1842 Pick 1896) but a better designation is chronic constrictive pericarditis (see Chapter 27) Sometimes the process may be slight without handicap from the nonconstricting or only slightly constricting pericardial adhesions

Tuberculosis of the blood vessels may occur in rare instances causing endarteritis granulomata and even aneurysmal dilatations The invasion may be either from the blood stream or from infected tissue (lymph nodes for example) contiguous to aorta or other blood vessel

The introduction of streptomycin has given promise of aid in a few instances of tuberculous pericarditis this drug in the dosage of 2 to 4 gm daily

has been apparently helpful but its toxic effects are a distinct drawback (see page 403 in Chapter 15)

The relationship of heart disease to tuberculosis of the lungs It has long been said that pulmonary tuberculosis is rare if there is considerable mitral stenosis This appears to be true the reason is not clear but it may be that the chronic pulmonary congestion resulting from mitral stenosis makes it difficult for the tubercle bacillus to gain a foothold In one series of 300 cases of mitral stenosis there was found but one case of pulmonary tuberculosis (0 3 per cent) and in a series of 20 000 cases of pulmonary tuberculosis there was reported to be but one case of mitral stenosis (0 005 per cent) (Montenegro 1919) Valvular heart disease of other sort (not marked mitral stenosis) is however occasionally and incidentally seen in pulmonary tuberculosis the combination was reported in 29 out of 1 097 cases of pulmonary tuberculosis valvular heart disease or both examined post mortem (Calthrop 1920) in 31 out of a series of 13 000 cases of pulmonary tuberculosis (Kellner 1921) and in 0 9 per cent of 7 115 necropsies on tuberculous patients (Brown quoted by Hawes 1932) An analysis of 522 adults with pulmonary tuberculosis revealed 3 cases of rheumatic heart disease and 2 of congenital heart disease (Buckingham and Hoffman 1935)

In contrast to the rarity of pulmonary tuberculosis in cases of pronounced mitral stenosis it is said to be rather a usual development in congenital stenosis of the pulmonary orifice (Austrian 1933) In this regard it is of interest that just the opposite conditions exist in the pulmonary circulation with these two lesions in mitral stenosis the pulmonary circulation is engorged and in pulmonary stenosis it is depleted

Much more important than the possible protective action of mitral stenosis in the case of phthisis is in rare cases the deleterious effect of extensive pulmonary tuberculosis on the heart This is not the production of the familiar so-called drop or vertical (or atrophied) heart which is sometimes seen in the more slender victims of tuberculosis with low diaphragm and general atonic state such a drop heart is of little or no importance in itself Rather is it the strain on the right ventricle resulting from increased pressure produced in the pulmonary circulation by obstruction caused by extensive destruction of pulmonary tissue fibrosis and pleural adhesions This strain may eventually in a few cases produce some right ventricular enlargement rarely to a considerable degree and not marked enough to cause definite increase beyond the normal in the percussion or roentgen ray size of the heart so that the change may easily escape notice In a very few cases actual failure of the right ventricle may occur but this is much rarer than in the case of chronic pulmonary fibrosis and emphysema of other cause which will be discussed in Chapter 20 During life there may be a great variety of size and shape of the heart shadow in the presence of active pulmonary tuberculosis (Porter and Gordon 1937)

Finally it is to be recognized that in patients with active tuberculosis in the lungs or elsewhere there is commonly as in the case of other infections

a certain degree of neurocirculatory asthenia with dyspnea palpitation and heartache which may on hasty analysis be wrongly ascribed to heart disease or to a toxic effect of tuberculosis of the heart

The course prognosis and treatment of tuberculosis of the heart and pericardium resolve themselves primarily into those of the underlying tuberculosis be it miliary pulmonary or of the nature of polyserositis The prognosis is always grave though some cases recover this number has increased somewhat since the introduction of streptomycin A pericardial effusion may need to be tapped and cases of chronic constrictive pericarditis may require surgical relief by pericardial resection Active tuberculosis of pericardium and heart must be treated by rest and good nursing care and a trial of streptomycin just as in the case of active pulmonary tuberculosis but the prognosis is always serious

EPIDEMIC CEREBROSPINAL MENINGITIS

Meningococcus infection may in rare cases involve the heart and cause an acute bacterial endocarditis or pericarditis as noted in Chapter 15 but such cardiac involvement is now largely preventable or amenable to recovery by the use of chemotherapy Meningococcic myocarditis has also been reported (Saphir 1936)

GONORRHEAL INFECTION

Acute or chronic gonorrhea may in rare cases infect the heart especially following gonorrheal arthritis or a virulent illness of other nature due to the same organism The involvement occurs in the form either of acute or of subacute bacterial endocarditis and is no longer as it once was fatal the newer chemotherapy being a specific remedy in most cases

OTHER BACTERIAL DISEASES INCLUDING SEPTIC INFECTIONS

Erysipelas septic infections and pyemia due to streptococcus or staphylococcus used to be occasional causes of acute bacterial endocarditis septic (purulent) pericarditis and myocardial abscesses Generally these were but terminal manifestations and were not responsible for death but sometimes they constituted the chief or most important part of the disease Treatment used to be of little avail when the heart itself was diseased but both prevention and recovery of cardiac and pericardial complications now may follow the use of the antibiotics (especially penicillin) and of the sulfonamide drugs aided by pericardiotomy and drainage in the case of purulent pericarditis

RICKETTSIAL DISEASES

Typhus fever Myocardial lesions and vascular disease (endarteritis) may result from exanthematic typhus fortunately now rare in civilized countries at peace they are as a rule of little or no significance Transient *T* wave ab-

normalities in the electrocardiogram are common during the acute infection (Norvut 1947) Complete arterial obstruction and gangrene may however complicate a few cases The toxicity and vasomotor paralysis resulting from this infection may kill but involvement of the heart is probably not responsible for death Endocarditis and pericarditis do not occur except from a secondary infection

Another important rickettsial disease which has been found even more constantly to be associated with myocardial involvement namely *tsutsugamushi fever* or *scrub typhus* was studied during World War II A large proportion of electrocardiograms of cases of scrub typhus has shown abnormalities chiefly in the T waves with recovery in most cases

Rocky Mountain spotted fever also falls into the group of rickettsial diseases and may affect the myocardium during the acute illness

VIRUS DISEASES

An interesting and important advance in our knowledge of the effect of infections on the heart has taken place during recent years in the field of the virus diseases In most instances the victims of such infections escape any serious cardiac injury but in a certain number of instances rare as a rule the myocardium may be seriously affected Virus pericarditis has also of late been identified

Influenza had long been suspected and by some so incriminated but only in the last few years has actual proof been presented (Finland et al 1945) It is quite possible that lesser lesions of the heart muscle have often resulted from influenza but serious or fatal myocarditis is rare Most of the symptoms which years ago were attributed to such a condition were characteristically those of a fatigued state or neurocirculatory asthenia which so often complicates the convalescence from any infection (see Chapter 22)

Mumps has been shown to produce temporary atrioventricular block in rare cases clearing with convalescence (Rosenberg 1945)

German measles (rubella) has been shown to have in many instances a serious effect on the eyes and heart of a fetus if it attacks the mother during the first three months of pregnancy (Gregg 1941 Swan 1943)

Yellow fever may give rise to nonspecific myocardial inflammation and degeneration in fatal cases (Cannell 1928)

Poliomyelitis Recently myocardial changes characterized by perivascular infiltration of lymphocytes and neutrophiles have been reported in 6 out of 7 cases with poliomyelitis who died suddenly during the acute or convalescent stages (Saphir and Wile 1942) and several other observers have confirmed these findings since (Gefter et al 1947 Ludden and Edwards 1948)

Infectious hepatitis and *infectious mononucleosis* have also been found to cause in some cases myocardial involvement as indicated electrocardiographically

Still other viruses need further appraisal in this respect

TRICHINIASIS

It was long known that trichiniasis may involve the myocardium as well as other muscles in the body but the possible frequency with which he trichinae invade the heart in well infested cases was not pointed out until 1935 (Spink 1935) A serious effect directly from this heart involvement itself has not been found but changes in the electrocardiogram (flattening or inversion of the *T* waves low voltage of *QRS* waves and intraventricular block) in some cases (6 of 18 patients with myocardial trichiniasis in Spink s series) may justifiably be attributed to the presence of the parasites in the heart muscle In another series of 44 cases of trichiniasis of mild type however only 2 showed possible clinical evidence of myocardial involvement (Beecher and Amidon 1938) There is no specific therapy

TRYPANOSOMIASIS

A cause of heart disease in South America (especially in Brazil) rare or nonexistent elsewhere namely cardiac trypanosomiasis has been frequently reported in recent years following its discovery in human beings by Chagas in 1909 This consists of the invasion of the myocardium in childhood b trypanosomes (Figure 91 illustration below) with foci of inflammatory reaction which later lead to cardiac weakness and failure and arrhythmias in



FIG 91 Microphotograph showing myocardial trypanosomiasis (Chagas disease) Note Trypanosoma cruzi near the center of the field (Kindness of Drs C Chagas and R Menezes Brazil and Frank Wilson Ann Arbor Michigan)

middle life Sudden death may result The pericardium endocardium and valves are not involved but the myocardium is said to be more often involved than in any other disease In the chronic cases multiple areas of fibrosis may be found scattered through the heart muscle Thousands of cases of this remarkable type of heart disease have been seen in Brazil but it has not yet been encountered in the United States or Europe

ECHINOCOCCUS DISEASE

Infection with the echinococcus may involve the heart and a number of cases of hydatid cysts in or attached to the walls of atria and of ventricles or interventricular septum have been reported It is usually but a part of general echinococcus disease I have encountered such cases in Greece (1948)

ACTINOMYCOSIS

Actinomycosis of heart and pericardium is a very rare infection Thirty years ago the case of a man 34 years old was reported with initial lesion in the esophagus and secondary invasion of the heart pericardium lung and pleura It was noted that twenty two other cases had been described previously (Letulle and Hufnagel 1919)

INTESTINAL PARASITES

Most of the parasites that invade the intestinal tract of man do not affect the heart these include the roundworm (ascaris) the pinworm (oxyuris) and the ordinary tapeworms (taenia saginata and taenia solium) but the hook worm (ankylostoma) and less commonly the fish tapeworm (dibothrio cephalus latus) may by their production of severe anemia cause an important degree of cardiac dilatation and loud murmurs (see Chapter 23)

OTHER INFECTIONS AND INFESTATIONS

A few other diseases may involve the heart for example Brucella meli tensis (Malta fever) sarcosporidial infection of the myocardium filariasis (with ova found in the heart) strongyloidiasis cardiac heterophydiasis (in festation with flukes from raw fish) and cysticercosis of the myocardium (and brain) In the sixteenth century there were frequent reports of worms in the chambers of the human heart before the days when it was recognized that these supposed worms were actually elongated blood clots both ante mortem and post mortem it is however true that the dog s heart may contain worms (*Dirofilaria immitis* see Query *J A M A* 1924 CIII 1728) which intro duced by insect bite go through a cycle of development and then migrate in adult life along the veins into the right heart chambers where by their accumu lation en masse the individual thread like filaria attaining the length of one to two feet, may actually block the circulation and cause pulmonary embolism

Rheumatoid arthritis periarteritis nodosa and conditions like lupus erythe-

matosus allied to these are quite frequently attended by heart disease but it is still difficult or impossible in view of our ignorance as to their etiology to label them as infections or even reactions to infections or toxic states (see Chapter 23)

FOCAL INFECTIONS

Focal infections may have a deleterious effect on the heart either directly or indirectly Actual cardiac disease of the nature of bacterial endocarditis is known to follow an acute focal infection like that of tonsil of middle ear or of skin But this happens only rarely except in the case of dental infections and extractions which almost certainly are a very important source of entry of the Streptococcus viridans into the body to inaugurate the grave infection of subacute bacterial endocarditis in cases of rheumatic or congenital heart disease (see Chapter 15) it behooves us in such cases to use the greatest vigilance in avoiding strain from too much operative work at any one time and in combating the serious results of dental and other focal infections by the use of the antibiotics (in particular penicillin) and of the sulfonamide drugs and otherwise

How frequently slight myocardial damage or a mild endocardial lesion with recovery may occur with such focal infections we do not know but there exists no proof that this is even an occasional happening We do know that heart disease already existing is sometimes aggravated by the presence of focal infections with the appearance of arrhythmia or of symptoms of congestive failure or angina pectoris or with their increase if already present Whether or not there is actual heart disease cardiac arrhythmia may be set off or aggravated by focal infections such arrhythmia is as a rule entirely unimportant in itself *consisting of premature beats (extrasystoles) or paroxysms of tachycardia* but sometimes it may comprise atrial fibrillation or flutter or prolonged paroxysmal tachycardia Among the focal infections which may precipitate or aggravate cardiac arrhythmia congestive failure or angina pectoris are chronic cholecystitis prostatitis pyelitis colitis infection of gums apical tooth abscesses frontal sinusitis lung abscesses and other similar troubles

Correction of these focal infections by surgery or by other measures (if the circulatory condition permits) may relieve the patient of his temporary state of ill health or at least cause improvement the risk of such corrective procedures is usually justified provided too much is not attempted at one time (the removal of more than one or two infected teeth at one sitting for example, may result in vasomotor shock or may itself precipitate heart failure and death) The wisest course then is to view focal infections so far as the heart is concerned neither with overmuch fear nor with excessive disregard to consider them as possible important factors producing a state of ill health which may cause strain on the heart and to eradicate them if possible and feasible However it is a mistake to perform an operation of choice and not of necessity for example to remove a symptomless gallstone (or to correct surgically a

simple inguinal hernia) in the face of severe angina pectoris or of congestive failure

INFECTIONS NOT CAUSING HEART DISEASE

Many infections never cause heart disease although they may precipitate such trouble as failure or atrial fibrillation in hearts already diseased or they may be attended by complicating infections which do cause heart disease This is particularly true of most of the contagious diseases of childhood whooping cough (pertussis) chickenpox (varicella) and measles (rubeola) The acute respiratory tract infections—rhinitis sinusitis pharyngitis laryngitis tracheitis and bronchitis—do not of themselves cause heart disease, but like tonsillitis they may occasionally precipitate the rheumatic infection which does almost always damage the heart The same statement is true of otitis media but infections of the gastrointestinal and genitourinary tracts very rarely precipitate any heart trouble

BIBLIOGRAPHY

DIPHTHERIA SCARLET FEVER TUBERCULOSIS OTHER INFECTIONS AND INFESTATIONS

Diphtheria

Alstead S "The Heart After Diphtheria *Lancet* 1933 I 413

Engle M A "Recovery from Complete Heart Block in Diphtheria *Pediatrics* 1949 III 222

Gore I Myocardial Changes in Fatal Diphtheria Summary of Observations in 221 Cases" *Am J M Sc* 1948 CCXV 257

Hume W E and Clegg S J "A Clinical and Pathological Study of the Heart in Diphtheria *Quart J Med* 1914 VIII 1

Jones T D and White P D "The Heart After Severe Diphtheria" *Am Heart J* 1927 III 190

Kay C F and Livingood C S Myocardial Complications of Cutaneous Diphtheria" *Bull U.S Army M Dept* 1945 IV 46

Metropolitan Life Insurance Co Health Contrast World Wars I and II *Statist Bull* 1942 XXIII No 3

Perry C B Persistent Conduction Defects Following Diphtheria *Brit M J* 1939 I 117

Sutherland J., and Willis R A "Endocarditis Due to Diphtheroid Bacillus Structurally and Culturally Resembling Diphtheria Bacillus *J Path & Bact* 1936 XLIII 127

Thompson W P Golden S E and White P D "The Heart Fifteen to Twenty Years After Severe Diphtheria" *Am Heart J* 1937 XIII 534

Warthin A S "The Myocardial Lesions of Diphtheria" *J Infect Dis* 1924 XXXV 32

Scarlet Fever

Faulkner J M Place E H and Ohler W R "The Effect of Scarlet Fever on the Heart," *Am J M Sc* 1935 CLXXXIX 352

Neubauer C "Cardiac Complications in Scarlet Fever *Arch Dis Child* 1945 XX 81

Paul J R Salinger R and Zuger B "The Relation of Rheumatic Fever to Post scarlatinal Arthritis and Postscarlatinal Heart Disease—A Familial Study" *J Clin Investigation* 1934 XIII 503

Shookhoff C and Taran L M Electrocardiographic Studies in Infectious Diseases II Scarlet Fever" *Am J Dis Child* 1931 XLII 554

Pneumonia

Cohn A E and Jamieson R A 'The Action of Digitalis in Pneumonia *J Exper Med* 1917 XXV 65
Master A M Romanoff A and Jaffe H Electrocardiographic Changes in Pneumonia *Am Heart J* 1931 VI 696
Saphir O and Amromin G D "Myocarditis in Instances of Pneumonia" *Ann Int Med* 1948 XXVIII 963

Typhoid Fever

Brow G R 'The Heart in Typhoid Fever *Canad M A J* 1929 XX 606
Mainzer F Electrocardiographic Study of Typhoid Myocarditis *Brit Heart J* 1947 IX 145
Porter W B and Bloom N 'The Heart in Typhoid Fever A Clinical Study of Thirty Patients *Am Heart J* 1935 X 793
Rachmilewitz M and Braun K Electrocardiographic Changes in Typhoid Fever and Their Reversibility Following Niacin Treatment *Am Heart J* 1948 XXXVI 284
Storti E Bobba P and Curti P C *Il Cuore nel Tifo Addominale* Typographia del Libro Pavia 1948

Tuberculosis

Anders J M "Tuberculosis of the Myocardium *J A M A* 1902 XXXIX 1081
Andrews G W S Pickering G W and Sellors T H 'The Aetiology of Constrictive Pericarditis with Special Reference to Tuberculous Pericarditis Together with a Note on Polyserositis *Quart J Med* 1948 XVII 291
Austrian C R Heart Disease and Its Relation to Tuberculosis *Mod Concepts Cardiovas Dis* 1933 II No 3
Baker R D Endocardial Tuberculosis *Arch Path* 1935 XIX, 611
Buckingham W W and Hoffman J S Pulmonary Tuberculosis Associated with Valvular Heart Lesions *Missouri State M A J* 1935 XXXII 438
Calthrop G T "The Relation Between Valvular Disease of the Heart and Pulmonary Tuberculosis *Tubercle* London 1920 I 263
Chevers N Observations on the Diseases of the Orifice and Valves of the Aorta *Guy s Hosp Rep* 1842 VII 387
Hawes J B "The Heart in Pulmonary Tuberculosis" *New England J Med* 193 CCVII 874
Horn H and Saphir O Involvement of Myocardium in Tuberculosis Review of Literature and Report of Three Cases *Am Rev Tuberc* 1935 XXXII 492
Kellner F Herzklappenfehler und Lungentuberkulose *Ztschr f Tuberkulose* 1931 XXXV 33
Menon T B and Prasada Rao C K "Tuberculosis of the Myocardium Causing Complete Heart Block" *Am J Path* 1945 XXI 1193
Montenegro J V Mitral Stenosis and Pulmonary Tuberculosis *Arch espan d tisiologia* Barcelona 1919 I 89
Pick F Ueber chronische unter dem Bilde der Lebercirrhose verlaufende Pericarditis (pericarditische Pseudolebercirrhose) nebst Bemerkungen über die Zuckergussleber (Curschmann)" *Ztschr f klin Med* 1896 XXIX 385
Porter R E and Gordon W H "Size of the Heart in Pulmonary Tuberculosis" *Am Rev Tuberc* 1937 XXXVI 82
Raviart G "La tuberculose du myocarde *Arch d méd expér* 1906 XVIII 141
Schnitzer R "Myocardial Tuberculosis with Paroxysmal Ventricular Tachycardia *Brit Heart J* 1947 IX 213
Thompson W P "Primary Tuberculosis of the Pericardium" *J.A.M.A* 1933 C, 64..
Wilbur E L "Myocardial Tuberculosis Cause of Congestive Heart Failure" *Am Rev Tuberc* 1938 XXXVIII 769

Other Bacterial Infections

Bien C W and Tung C L Electrocardiographic Changes in Cholera *Chinese M J* 1933 XLVII 662
Call J D Baggenstoss A H and Merritt W A "Endocarditis Due to Brucella Report of 2 Cases *Am J Clin Path* 1944 XIV 508
Firestone G M Meningococcus Endocarditis *Am J M Sc* 1946 CCXI 556
Saphir O Meningococcic Myocarditis *Am J Path* 1936 XII 677
Whitehill M R Longcope W T and Williams R "The Occurrence and Significance of Myocardial Failure in Acute Hemorrhagic Nephritis *Bull Johns Hopkins Hosp* 1939 LXIV 83

Rickettsial Diseases

Gubergritz M M Zur Klinik der Herzstorungen als Folge des Fleckfiebers *Klin Wchnschr* 1926 V 845
Halonen P I "Uber die Veranderungen im Elektrokardiogramm und im Herzmuskel bei Epidemischem Flecktyphus *Acta soc med Fennicae Duodecim* 1945 XXXIV 90
Levine H D "Cardiac Complications of Tsutsugamuschi Fever (Scrub Typhus) An Investigation of Their Persistence *War Med* 1945 VII 76
Norvut, L Electrocardiogram in Typhus *Acta med Scandinav* 1947 CXXVI 565

Virus Diseases

Adler E and Lyon E "Herzstorungen im Zusammenhang mit infektoser Hepatitis" *Cardiologia* 1946–47 XI 111
Cannell D E "Myocardial Degenerations in Yellow Fever" *Am J Path* 1928 IV 431
Dehn H Feil H and Rinderknecht R E Electrocardiographic Changes in Cases of Infectious Hepatitis *Am Heart J* 1946 XXXI 183
Dolgopol V B and Cragan M D Myocardial Changes in Poliomyelitis" *Arch Path* 1948 XLVI 202
Evans W F, and Graybiel A Electrocardiographic Evidence of Cardiac Complications in Infectious Mononucleosis" *Am J M Sc* 1946 CCXI 220
Felknor G E and Pullen R L Mumps Myocarditis *Am Heart J* 1946 XXXI 238
Finland M Parker F Jr Barnes M W and Joliffe L S Acute Myocarditis in Influenza A Infections Two Cases of Nonbacterial Myocarditis with Isolation of Virus from the Lungs *Am J M Sc* 1945 CCIX 455
Gefter W I et al "The Heart in Acute Anterior Poliomyelitis" *Am Heart J* 1947 XXXIII 228
Gregg N M Congenital Cataract Following German Measles in the Mother" *Tr Ophth Soc Australia* 1941 III 35
Ludden T E and Edwards J E Carditis in Poliomyelitis An Anatomic Investigation of 35 Cases and Review of the Literature" *Proc Staff Meet Mayo Clin* 1948 XXIII 379 and *Am J Path* 1949 XXV 357
Rosenberg D H Acute Myocarditis in Mumps *Arch Int Med* 1945 LXXVI 257
Saphir O Virus Myocarditis *Mod Concepts Cardiovas Dis* 1949 XVIII No 6
Saphir O and Wile S A. Myocarditis in Poliomyelitis" *Am J M Sc* 194 CCIII 781
Spain D M Bradess V A and Parsonnet V "Myocarditis in Poliomyelitis" *Am Heart J* 1950 XL 336
Swan C Tostevin A L Moore B Mayo H and Barham Black G H "Congenital Defects in Infants Following Infectious Diseases During Pregnancy With Special Reference to the Relationship Between German Measles and Cataract, Deaf Mutism Heart Disease and Microcephaly and to the Period of Pregnancy in Which the Occurrence of Rubella Is Followed by Congenital Abnormalities" *M J Australia* 1943 II, 201

Swan C Tostevin A L and Black G H B "Final Observations on Congenital Defects in Infants Following Infectious Diseases During Pregnancy with Special Reference to Rubella *M J Australia* 1946 II 889

Malaria

Merkel W C "Plasmodium Falciparum Malaria Coronary and Myocardial Lesions Observed at Autopsy in Two Cases of Acute Fulminating P Falciparum Infection" *Arch Path* 1946 XLI 290

Rojas R A and Deza D "Cardiac Changes in Malarial Patients *Am Heart J* 1947 XXXIII 702

Sprague H B "The Effects of Malaria on the Heart *Am Heart J* 1946 XXXI 4 6

Infestations

Arrillaga F C de Soldati L and Gandulla L Sobre cuatro casos de miocarditis chagasica cronica" *Rev argent de cardiol* 1950 XVII 29

Baker R D and Brian E W "Blastomycosis of the Heart Report of Two Cases. *Am J Path* 1937 XIII 139

Beecher C H and Amidon E L "Electrocardiographic Findings in 44 Cases of Tri hi nosis *Am Heart J* 1938 XVI 219

Carter M G and Korones S B "Amebic Pericarditis Review of the Literature and Report of a Case" *New England J Med* 1950 CCXLII 390

Chagas C and Villela E Forma cardiaca da Trypanosomiase Americana" *Memorias do Instituto Oswaldo Cru* 1922 XIV No 1 Reprinted by Manguinhos Rio de Janeiro 1922

Cornell A and Shookhoff H B "Actinomycosis of Heart Simulating Rheumatic Fever Report of 3 Cases of Cardiac Actinomycosis with Review of Literature" *Arch Int Med* 1944 LXXIV 11

Cruz O and Chagas C First description of American trypanosomiasis in Brazil 1909 (see Foreign Letters *J A M A* 1943 CXXI 65)

Cuenca H "La miocarditis Bilharziana" *Rev Cubana d Cardiol* 1938 I 25

d Abreau A L "Removal of a Hydatid Cyst from Wall of Left Ventricle *Thorax* 1950 V 362

Decourt L V et al "Chronic Heart Involvement in Chagas Disease" *Am Heart J* 1947 XXXIII 697

Dobrotin A N Drei Fälle des Echinokokkus des Herzens" *Virch Arch f path Anat* 19 6 CCLXI 575

Gilmore H R Jr et al Sarcosporidiosis with Parasites Found in Heart Case" *Am J Trop Med* 1942 XXII 121

Kyle L H McKay D G and Sparling H J "Strongyloidiasis *Ann Int Med* 1948 XXIX 1014

Letulle M and Hufnagel M "L actinomycose du coeur" *Bull d l'Acad d med d Paris* 1919 LXXXII 170

MacNeal W J Blevins A and Duryee A W Clinical Arrest of Endocardial Actinomycosis After Forty four Million Units of Penicillin" *Am Heart J* 1946 XXXI 668

Reingold I M Myocardial Lesions in Disseminated Coccidioidomycosis" *Am J Clin Path* 1950 XX 1044

Rio Leon R "Contribucion al estudio de las manifestaciones cardiovasculares de la ankilostomiasis" *Rev Cubana d Cardiol* 1943 IV 25

Spink W W "Cardiovascular Complications of Trichinosis" *Arch Int Med* 1935 LVI 238

Zoeckler S J Cardiac Actinomycosis A Case Report and Survey of the Literature" *Circulation* 1951 III 854

CHAPTER 18

THE HEART IN THYROID DISEASE AND IN DISEASES OF OTHER GLANDS OF INTERNAL SECRETION

Although this chapter requires less revision since the last edition than most of the rest of the book it is like several other chapters decreasing in importance and quite likely can be eliminated altogether eventually or at least demoted to a small section in the chapter on miscellaneous etiologic relationships This is of course due to the constantly earlier recognition and more adequate treatment of endocrine diseases before the heart and blood vessels are importantly affected

Endocrinopathy has very little serious effect on the heart Even that disorder which has much more influence than any other namely thyrotoxicosis now accounts for but a small fraction of 1 per cent of cases of heart disease in any enlightened community However there are many interesting and important cardiovascular and circulatory relationships and effects of the endocrine hormones normally and abnormally For example the glands of internal secretion especially the adrenal the posterior pituitary and the thyroid have an important influence on the distribution of water throughout the body partly by a direct effect on the kidney and cell permeability in general and partly by an effect on electrolytes and metabolism of carbohydrates protein and fat The adrenal and possibly the posterior pituitary play an important role in the renal control of sodium and upon its internal distribution Transfers of sodium and potassium across cell membranes are influenced by the hormones And now the hormones are being studied as to their striking influence on the course of certain diseases such as rheumatoid arthritis and rheumatic fever A great deal of study remains to be done on these relationships but they are opening up an important field which may as a matter of fact result eventually in a considerable revision of a book such as this Further discussions of hormonal influences will be found elsewhere in the book for example later in the present chapter in the discussion of adrenal diseases and in the chapters on rheumatic fever and congestive failure

DISEASES OF THE THYROID GLAND

Diseases of the thyroid gland which materially affect the heart are or that which produces an excessive or toxic secretion (exophthalmic goiter Graves disease) resulting in thyrotoxicosis, and that which is attended l a markedly decreased secretion (myxedema and cretinism)

Simple enlargement of the thyroid gland (colloid or simple or endem goiter) causes no trouble with the heart or circulation unless the gland becom so large that pressure on veins and arteries results in embarrassment to th entrance of blood into and its exit from the heart or compression of trache and bronchi interferes with respiration (Rose 1878 Kocher 1902) Adenom atous goiter (struma nodosa) is much more likely to cause these disturbance than is simple colloid goiter In some parts of the world for example in th north central (middle west) and northwestern regions of the United State bordering on the Great Lakes and westward to the Pacific Ocean and i Switzerland colloid or simple goiter with its occasional slight secondar circulatory embarrassment is common in other parts of the world for ex ample in New England and in other lands bordering the sea where iodine plentiful such goiter is rare

Excessive secretion is not produced by a colloid goiter but if later in lif the simple colloid goiter becomes adenomatous thyrotoxicosis may be super imposed

THE HEART IN THYROTOXICOSIS

Thyrotoxicosis also called hyperthyroidism may result from general hyper plasia or from adenomatous goiter The term thyrotoxicosis will be used throughout the book in the place of hyperthyroidism since it indicates a toxic degree of hyperthyroidism and includes abnormal thyroid secretion if such exists as well as excessive secretion

Persistent overactivity of the thyroid gland commonly gives rise to an im portant but preventable type of heart trouble which has become familiarly known as the thyroid heart but which might better be called the thyrotoxic heart or the heart in thyrotoxicosis For the most part the heart as wel as the circulation in general in thyrotoxicosis is simply physiologically over active pathologic changes that is real heart disease in thyrotoxicosis is relatively rare The true thyrocardiac may be said to be the individual who as a result of thyrotoxicosis has atrial fibrillation and eventually if not properly treated cardiac enlargement and congestive heart failure as a rule the evolution of a thyrocardiac is in just that order

Frequency Thyrotoxic heart disease varies in frequency both absolutely and relatively in different parts of the world not only according to the fre quency of thyrotoxicosis in such parts but also according to the rapidity of diagnosis and proper treatment of the thyrotoxicosis In New England 20 to 25 years ago thyrotoxicosis was found to be a causative factor in 3 per cent of

2 314 cases of organic heart disease (White and Jones 1928) in Virginia it was reported in 3½ per cent of 300 cardiac patients (Wood Jones and Kimbrough 1926) while in Oregon it was found in 11 per cent of 1 344 cardiac cases (Coffen 1929) in Oregon there is much more endemic (colloid) goiter than in New England and Virginia out of all proportion to the amount of thyrotoxicosis that is the endemic goiter is relatively much more frequent than the thyrotoxicosis That thyrotoxic heart disease is preventable and is already decreasing in communities where early diagnosis and adequate treatment of the thyrotoxicosis itself are carried out is indicated by the fact that among the first 2 500 patients whom I examined in consulting practice from 1920 to 1927 because of cardiac symptoms or signs there were 24 cases of heart disease due to thyrotoxicosis while among the next 2 500 patients seen from 1927 to 1933 there were only 10 such cases in the third lot of 2 500 private patients seen from 1933 to 1940 there were 4 cases and in the fourth such series examined from 1940 to 1946 there were but 3 thyrotoxicosis not responsible for heart disease was occasionally found throughout the entire period

Etiology *Cause* The fundamental cause of this type of heart disease is an abnormal activity of the thyroid gland with excessive (or disturbed) secretion The mechanism by which thyrotoxicosis produces heart disease is probably dependent on three factors which may be summarized briefly as follows First the increased general body metabolism which results from abnormal thyroid activity increases the demand on the heart and circulation It has been estimated that the blood flow at rest is at least 50 per cent above the normal in a case of thyrotoxicosis of average intensity and that with exercise this disproportion is still greater The increased blood flow is due not only to the increased pulse rate but also to an increase of volume output per beat from the heart although this increase of volume output per beat is less than in a normal heart responding to exercise with the same degree of tachycardia as that found in thyrotoxicosis The systolic blood pressure is somewhat elevated and the diastolic pressure often lowered so that the pulse pressure is frequently much increased This constantly increased blood flow is maintained by a constant overactivity of the circulation Such persistent overactivity tends to increase somewhat the size of the heart both in muscle (thus producing a simple work hypertrophy) and in capacity (dilatation) but cardiac enlargement is very inconstant and not the rule in the majority of cases Eventually in some very severe prolonged cases and in those complicated by valvular heart disease hypertension or coronary disease the persistent overactivity can cause excessive strain arrhythmia and failure A possible parallelism has been seen in experimental animals which show considerable cardiac enlargement after excessive exercise maintained during much of the time for weeks or months

A second and more important consideration however is that practically all thyrotoxic heart disease starts with a persistent atrial fibrillation the tachycardia and arrhythmia of atrial fibrillation add to the strain of the thyrotoxicosis and tend after some years to produce cardiac enlargement which might

not have occurred from atrial fibrillation in the case of a normal heart to start with without thyrotoxicosis particularly if the ventricular rate were adequately controlled by digitalis (an impossibility in the presence of considerable thyrotoxicosis) A third factor that helps to explain the heart disease in thyrotoxicosis is that the heart itself is the seat of specific thyroid stimulation with local increased metabolism as in the case of other tissues in the body this increased wear and tear of the cells of the myocardium favoring in its turn enlargement and failure A fourth possible factor is that of a kind of arteriovenous shunt or aneurysm with blood rushing through the widely dilated vessels of the thyroid gland affording an appreciable extra burden for the heart and favoring enlargement as in the case of a traumatic arteriovenous aneurysm anywhere (Boas 1923)

An actual myocardial lesion consisting of degenerative changes at one time suggested as an important finding, has been in more recent years discounted and shown to be but an inconstant incidental occurrence (McEachern and Rake 1931 Weller and associates 1932)

A distinction so far as the heart is concerned between general glandular hyperplasia and the so called adenomatous goiter with hyperfunction (toxic adenomata) cannot be made as a rule the latter is found in older patients in whom other causes of heart strain (such as hypertension and coronary disease) are also more likely

The frequency of definite cardiac abnormality (not simply tachycardia and cardiac symptoms) in patients with thyrotoxicosis has been reported variously from a high estimate of enlargement of the heart in 50 to 60 per cent of fatal cases (McEachern and Rake 1931 Kepler and Barnes 1932) to a low estimate of only a few per cent in unselected groups atrial fibrillation in about 15 per cent and cardiac insufficiency in 5 to 10 per cent These abnormalities of the heart are much more common when there are complicating factors like hypertension

Age The age at which thyrotoxicosis is found varies widely, from 3 years up to 76 but the commonest age of onset is from 20 to 40 years In a series of 500 cases of thyrotoxicosis analyzed by Means and Richardson (1929) the age incidence of onset by decades was as follows first decade 3 cases second 60 third 165 fourth 147 fifth 93 sixth 29 and seventh 3 The average age was 37 years in another series of 500 cases of thyrotoxicosis (Hurxthal 1928) The age incidence of thyrotoxic heart symptoms parallels this more or less closely in a series of 68 cases 56 per cent were between 30 and 50 years old (White and Jones 1928) In a series of 108 cases of thyrotoxicosis with atrial fibrillation the average age was 51 5 years (Barker Bohning and Wilson 1932) these represent the more advanced cases on the way to serious thyrotoxic heart disease

Sex In thyrotoxicosis itself the female sex predominates over the male the ratio is about 5 to 1 In Means and Richardson s series (1929) of 500 cases of thyrotoxicosis there were 417 females and 83 males But the males are

involvement (by about 2 to 1) in a series of 34 cases of my own of thyrotoxic heart disease there were 24 women and 10 men

Other etiologic factors Race has little to do with thyrotoxic heart disease but in days gone by social and economic status did play a role in that inadequate financial resources did at times prevent early diagnosis and surgical correction of the thyrotoxicosis and so favored the establishment of heart disease In thyrotoxicosis itself heredity plays a part how important we do not know

In the incidence of simple nontoxic goiter and perhaps secondarily in that of toxic goiter there is a role played by geographic factors involving iodine content of foods and water Heart trouble due to thyrotoxicosis is more common in regions where there is much simple goiter but this is not due to the goiter itself The change of the simple goiter later in life to adenomata which can become toxic may account for this finding

Finally the education and intelligence of both the lay and medical population determine the rapidity with which the thyrotoxicosis is detected and corrected—a factor of very great importance in the prevention of heart disease

Pathology There are no constant cardiovascular lesions in thyrotoxicosis Enlargement of the heart with hypertrophy of the fibers is present in many cases especially in those with long-established atrial fibrillation but it is sometimes difficult to exclude the factors of hypertensive and coronary heart disease in these cases In a few cases necrosis of the myocardium has been found but this finding has not been confirmed as a thyroid effect The heart weight is generally somewhat increased to 400 or 500 gm in serious cases the average weight of the hearts of 13 fatal cases was 438 gm the two heaviest hearts weighing 530 gm each (Barker Bohning and Wilson 1932) With the onset of failure dilatation of the cavities and atrioventricular valve rings occurs but endocarditis and pericarditis are not found as a primary result of thyroid toxicity

Symptoms There are no characteristic symptoms of thyrotoxic heart disease The early cardiovascular symptoms of thyrotoxicosis itself are due to the tachycardia and effort syndrome they are chiefly palpitation and dyspnea and uncommonly heartache If atrial fibrillation or failure supervenes these symptoms increase Palpitation is of two types (1) the forceful beating with normal heart rhythm which may be extremely unpleasant and (2) that due to paroxysmal changes in rhythm Periods of rapid palpitation are common in thyrotoxicosis whether or not the heart is diseased they last a few minutes to a few hours and are due to paroxysms of sinoatrial or ectopic atrial tachycardia or of atrial fibrillation or flutter Angina pectoris rarely accompanies thyrotoxicosis and then only in older persons in whom the stage is already set by the presence of coronary disease which is not sufficient in itself to give rise to the paroxysmal pain The angina pectoris like the arrhythmia and congestive failure may be relieved by thyroidectomy when the metabolic rate is reduced thereby

Signs Increased heart action both in rate and force is the most common

cardiovascular sign in thyrotoxicosis and this activity is manifest on inspection palpation and auscultation over the precordium on inspection and palpation of the arterial pulse in neck and arms and on fluoroscopic examination Enlargement of the heart congestive failure and arrhythmia when they occur show themselves in the usual way In the early stage of the disease the heart may at first appear to be enlarged on hasty inspection and palpation because of the forceful beating against the chest wall when really it is of normal size Cardiac hypertrophy has however been found at autopsy in the majority of fatal cases (Friedberg and Sohval 1937) A harsh unusually superficial systolic murmur is sometimes heard in thyrotoxicosis in the second and third intercostal spaces just to the left of the sternum its origin is not clear but it is probably a physiologic pulmonary murmur dependent on the increased pulmonary circulation with dilatation of the pulmonary artery reinforced by the forceful heart action and thin chest wall This pulmonary systolic murmur has in rare cases been attended by a slight thrill Also at times a to and fro friction rub has been noted in the region of the pulmonary conus (Goodall 1920 Lerman and Means 1932) and in very rare cases a functional aortic regurgitant murmur has also been described (Parade 1935)

Exophthalmos and thyroid gland enlargement the most common signs of thyrotoxicosis may be but little evident in some cases and the heart action may first suggest the correct diagnosis A staring or worried look is sometimes present in the absence of frank exophthalmos lid lag may be present also with little exophthalmos Bulging of the eyes unilateral or bilateral may actually be precipitated or aggravated by thyroidectomy

In almost 80 per cent of cases of thyrotoxicosis the heart rhythm is normal and the pulse rate is fast averaging 100 to 120 per minute at rest Rare cases have a normal or only slightly elevated pulse rate In the remaining 20 per cent the heart rhythm is disturbed the disturbance consisting almost invariably of atrial fibrillation (noted in 207 of Ernstene s 1 000 cases 1938) of permanent nature in two thirds of the cases and of paroxysmal type in one third In addition there are relatively infrequent cases with atrial flutter and atrial paroxysmal tachycardia

Atrial fibrillation is commonest in the cases with congestive failure occurring in the majority of these *in one series of 111 cases of thyrotoxicosis* with congestive heart failure atrial fibrillation was present in 83 per cent (Hurxthal personal communication 1930) Of 232 cases of atrial fibrillation due to thyrotoxicosis Hurxthal found that 38 per cent had also congestive failure Thus atrial fibrillation may be considered to be but a stepping stone to congestive failure an argument against such an actual entity as thyroid myocardial disease since atrial fibrillation often occurs without evidence of disease in the heart muscle In Ernstene s series of 1 000 cases of hyperthyroidism 44 (4 4 per cent) had congestive heart failure the two most important factors responsible for this complication were organic heart disease and uncontrolled atrial fibrillation

The systolic blood pressure is usually somewhat elevated in thyrotoxicosis

averaging 140 to 150 mm mercury in one quarter to one third of the cases it exceeds 150 The diastolic pressure is usually at a slightly decreased level averaging 60 to 70 mm Thus the pulse pressure is generally increased and the arterial pulse is full

The roentgen ray study of the heart in thyrotoxicosis shows often considerable prominence of the pulmonary artery (probably secondary to the marked increase in the pulmonary circulation) and unusually energetic rapid heart action these two signs are together very suggestive and almost pathognomonic of thyrotoxicosis especially with the subject in the resting state In spite of overactivity however the heart sometimes appears to be lacking in tone in the presence of thyrotoxicosis Aortic regurgitation also gives markedly increased cardiac action in a young person especially but the considerable cardiac enlargement and the aortic diastolic murmur make the differentiation easy the water hammer pulse is not so good a differentiating sign for in occasional cases of thyrotoxicosis with much peripheral vasodilatation there is a well marked Corrigan pulse If cardiac enlargement is present it is best made out by roentgenologic study Arrhythmias may be seen fluoroscopically but are not so well distinguished as by electrocardiography Unusual clearness of the lung fields has been noted as occurring in thyrotoxicosis probably largely because of the thin chest walls of most of the patients

The electrocardiogram shows no specific effect of thyrotoxicosis The tachycardia and arrhythmia that may be present are readily seen but the individual complexes are otherwise normal It was thought years ago that the *T* wave might be found unusually high because in hypothyroidism the *T* wave is always low but this has proved not to be the case in fact in many cases the *T* waves are low and in rare cases may actually be inverted in Lead 2 (Graybiel and White 1935) doubtless a sympathetic nervous effect it has been shown that sympathetic stimulation contrary to early ideas lowers or inverts the *T* waves while vagus stimulation raises them (Hartwell Burrett Graybiel and White 1942)

The basal metabolic rate during the active stage of thyrotoxicosis is always high though it varies considerably with the individual case being studied A rate of 50 to 75 per cent above normal is not infrequent 25 to 30 per cent above normal is considered to be on the borderline and demands close scrutiny for signs of thyrotoxicosis It must be remembered that careful technic and avoidance of excitement are essential before judgment can be passed confidently on a borderline case or even on one that shows a distinctly high rate Also it is important that repeated basal metabolic rate determinations should all show high readings in confirmation of the diagnosis of thyrotoxicosis one or two readings in doubtful cases are inadequate Congestive heart failure alone may definitely raise the basal metabolic rate to about +30 per cent apparently as the result of increased work occasioned by the labored breathing it has been reported as high as 40 to 50 per cent above normal though such increase is unusual The pulse rate pulse pressure and blood flow are all usually increased proportionally to the rise of the basal metabolic rate Al

though operative relief or spontaneous remission of active thyrotoxicosis may occasionally leave behind some cardiac involvement especially atrial fibril lation symptoms and signs usually subside along with the metabolic rate It should be added that very rare cases of thyrotoxicosis may have basal metabolic rates within the normal range (0 to +10 per cent for example) such patients probably represent the small group of individuals who normally show low rates (−20 to −30 per cent) without myxedema Thus all evidence is necessary besides the basal metabolic rate in difficult diagnostic cases

Two more specific tests for thyrotoxicosis than the basal metabolic rate have been introduced in the past few years they consist of (1) the measure ment of the protein bound iodine in the blood which should normally not exceed 7 5 to 8 0 gamma per cent and (2) the calculation of radioactive iodine (I 131) uptake by the thyroid gland which should normally not exceed 50 per cent but which in thyrotoxicosis is much increased This latter test is much more accurate than either the former or the basal metabolic rate determination

One of the most important of all diagnostic clues is the rapid and favorable response of true thyrotoxicosis to iodine therapy

Course and prognosis The course and prognosis of thyrotoxic heart disease are extremely variable and depend on the severity and duration of the thyro toxicosis The abnormal condition of the heart may be scarcely noticeable and with the clearing up of the cause of trouble occasion no further symptoms and few or no signs With very severe thyrotoxicosis that has lasted for a long time heart disease may be evident by the presence of enlargement atrial fibrillation and congestive failure but there are infrequent exceptions when the heart may appear to be perfectly normal even after a good many years The usual case of average toxicity shows in the course of years heart changes that are more than functional if there is no operative relief or spontaneous remission death from heart failure may ensue in such cases after a few more years Of a series of 178 fatal cases of thyrotoxicosis 27 showed severe con gestive failure in 9 of which no other factor could be found than the thyro toxicosis alone (Kepler and Barnes 1932) Other complications such as pneu monia may intervene to end the story Now and again in wasted and pigmented aged individuals chronic heart disease can be traced back to a former thyro toxic state but is very likely to be wrongly interpreted as arteriosclerotic" if the thyrotoxicosis is still active in these cases operation or other specifi therapy should be carried out and may be expected to afford considerable relief

It is to be noted that thyrotoxicosis tends to recur after subtotal thyroidec tomy in about 10 per cent of the cases (Greene and Hurxthal 1941) hence the return of atrial fibrillation or other signs or symptoms during the years following operation should make one think of this possibility

Complications The commonest cardiac complication of thyrotoxicosis is atrial fibrillation which may occur at first as a functional disturbance alon

with little or no actual heart disease In the late stages of thyrotoxic heart disease congestive failure may supervene It is of much interest that in thyro toxicosis as in beriberi the cardiac output may continue to be increased well above the normal despite the presence of considerable congestive heart failure with elevated systemic venous pressure

Chronic rheumatic valvular disease is an occasional complication of thyro toxicosis and atrial fibrillation may lead to a diagnosis of one or the other condition when both are present Coronary heart disease may be another com plication in the older cases and the combination may produce angina pectoris Hypertension of high grade may also occur (in about 10 per cent of the cases) the systolic blood pressure in thyrotoxicosis itself rarely exceeds 160 mm mercury

Treatment The treatment of the heart condition resulting from thyrotoxi cosis is fourfold (1) therapy of the thyrotoxicosis (2) therapy of heart fail-ure (3) therapy of atrial fibrillation and (4) observation for recurrence of abnormal thyroid activity

The first of these therapeutic procedures namely the treatment of the thyro-toxicosis comes foremost in the consideration of almost every case because not only does this therapy control the cause of trouble but it actually may relieve without further therapy either or both of the serious complications congestive failure and absolute arrhythmia

After careful trial of other methods of treatment of active thyrotoxicosis (either ordinary exophthalmic goiter or adenomatous goiter) a good many authorities (e g Means et al personal communication 1951) still believe that the best therapy in the present state of our knowledge is subtotal thyroid ectomy Rest in bed and roentgen irradiation though they have been apparently effective in some mild cases are far less dependable in the long run and any delay of proper treatment may do harm

A useful measure in the preparation of patients for operation has been the administration of iodine for one to two weeks for example potassium iodide 5 gr (0 3 gm) once daily in saturated solution the 5 minims or grains contain ing 330± mg of iodine or Lugol s solution 10 minims (0 60 cc) containing 60 mg of iodine three times a day for ten days Iodine promotes the storage of thyroglobulin in the follicles and places a barrier in the way of escape of hormone from the gland (Lerman and Salter 1936) hence the high basal metabolic rate the fast pulse rate and all the symptoms of thyrotoxicosis are much abated and the patient is a better risk for operation Iodine therapy alone is not sufficient to control the thyrotoxicosis constantly except in a few mild cases It has also been shown that thiouracil will control the basal metabolic rate prior to operation in the dosage of 300 mg of propyl thiouracil daily and divided into three doses given eight hours apart this is continued until there has been much improvement in the patient s condition at which time it is wise to give 5 to 10 drops of saturated solution of potassium iodide daily for ten days along with the thiouracil ending with the surgical operation Thi

ouracil and related preparations have in some cases been used successfull in controlling thyrotoxicosis without operation, however toxic effects espe cially on the blood limit its use

Shortly after operation when the occasional stormy reaction has subside it is usually discovered that the heart condition is much improved if not and the thyrotoxicosis continues further treatment may be necessary With carefu preparation and the expert anesthesia and surgery that are essential for the best results remarkable benefits have been frequently secured even in case which were apparently hopeless because of heart failure and which have been considered generally as poor operative risks The relief of the thyrotoxicosis in such cases has proved far more important in the relief of the heart trouble than have remedies like digitalis and rest in bed directed to aid the heart condition alone It is to be noted further that iodine has far more effect than digitalis in reducing the pulse rate in the tachycardia of thyrotoxicosis per se in fact digitalis is almost invariably ineffective in this respect while iodine is nearly always at first effective

An ingenious therapeutic technic recently introduced for thyrotoxicosis consists of the use of irradiated iodine (I-131) orally adequate control of the disease has been effected without surgery a desirable achievement in cases where the cardiac status is precarious Incidentally as will be noted in the chapters on Coronary Heart Disease (Chapter 21) and on Congestive Heart Failure (Chapter 30) irradiated iodine (I 131) has been used effec tively by Blumgart et al (1948) to control both coronary and myocardial insufficiency through the production of a medical thyroidectomy

The therapy of the heart failure due to thyrotoxicosis consists primarily as noted above in the control of the thyrotoxicosis itself by the administration of iodine and operation rest digitalis and diuretics are additional therapeutic measures not very effective however, until the high metabolic rate has been reduced The tolerance of thyrotoxic patients for digitalis is usually quite marked and the therapeutic dose of this drug must be proportionately in creased sometimes as much as 50 to 100 per cent above the ordinary dosage in order to obtain any appreciable effect whether beneficial or toxic but only under careful observation

The third therapeutic measure consists of treatment of the atrial fibrillation that may complicate thyrotoxicosis There is little likelihood of control of this arrhythmia while thyrotoxicosis persists but there is a fair chance almost an even chance that relief of the thyrotoxicosis alone will relieve also the atrial fibrillation If it does not do so quinidine will restore normal rhythm in abo t half of the remaining postoperative cases in whom this arrhythmia persists, while digitalis can be used permanently to control the ventricular rate in the rest of the cases with persistent atrial fibrillation The method of administering digitalis and quinidine will be discussed in Chapters 30 and 33 of this book For paroxysms of atrial fibrillation either before or after thyroidectomy rations of quinidine sulfate (3 to 6 gr 0 18 to 0 36 gm three or four times daily) may be tried they are more likely to be successful after operation

Differential diagnosis Thyrotoxicosis as a cause of cardiac enlargement failure and atrial fibrillation must be differentiated particularly from rheumatic heart disease and essential hypertension Moreover when patients presenting obvious signs of rheumatic or hypertensive heart disease with congestive failure do not obtain relief from the usual therapeutic methods thyrotoxicosis should be suspected as a possible complication

The early stage of thyrotoxicosis before definite cardiac signs have developed is especially to be distinguished from neurocirculatory asthenia Its differentiation is not always a simple matter it is sometimes impossible when the basal metabolic rate is at the normal borderline and there is no definite exophthalmos or thyroid gland enlargement—most of such cases prove later not to have any definite thyrotoxicosis The differential diagnosis requires special care if one has to deal with a patient who has both neurocirculatory asthenia and a colloid goiter

Rare atypical cases with overactive thyroid glands are found without exophthalmos or goiter a slight staring anxious expression unexplained loss of weight diarrhea pigmentation of the skin and tachycardia may afford clues When in doubt the basal metabolic rate should always be determined and repeated as often as necessary and especially the protein bound iodine in the blood should be determined (normal = 4 0 to 8 0 gamma per cent) or the radioactive iodine uptake (normal = 20 to 50 per cent at the end of 48 hours) Finally a therapeutic test with iodine may be carried out (Means 1937)

HYPOTHYROIDISM MYXEDEMA HEART

The state of underactivity of the thyroid gland consisting typically of myxedema in adults and of cretinism in children is an infrequent condition itself and a still rarer cause of appreciable heart disease However in almost every case some abnormality of cardiac function is evident in the sluggish heart action and especially in the uniform flattening or inversion of all the *T* waves of the electrocardiogram (Figure 92A page 454) these abnormalities are corrected by thyroid therapy (Figure 92B) Enlargement of the x ray heart shadow sometimes at least due to pericardial effusion is also a usual finding in severe myxedema in some cases it is very striking while in others due to the wide range of the normal heart size it may become evident only in the process of taking serial roentgenograms It generally subsides under thyroid treatment with astonishing speed and degree (Figure 93 page 455) Arteriosclerosis likewise is frequent in myxedema

The term myxedema heart has been applied to a condition found in about three quarters of the cases of myxedema (Zondek 1918 1919 Fahr 1925 1927 1932 Fournier 1942) and this will be described below In many cases of myxedema however especially the milder ones it is difficult or impossible to make out any important abnormality of the heart caused directly by this glandular deficiency The cretin too has no very definite heart disease but

shows as in myxedema, abnormal electrocardiographic *T* waves and sluggish cardiac action

Etiology *Cause* It is evidently the lack of sufficient thyroid secretion in myxedema which occasionally causes definite heart trouble in the form of enlargement or weakness or pericardial effusion for the administration of rations of thyroid gland corrects this trouble In what way the hypothyroidism causes this cardiac abnormality, and what other factors may favor this effect we do not know

Myxedema itself is usually of unknown origin but infrequently it follows thyroidectomy which is carried out to cure thyrotoxicosis Myxedema was intentionally produced about 18 years ago in a new treatment of intractable angina pectoris and myocardial insufficiency by the surgical operation of total thyroidectomy (see Chapters 21 and 30) but this form of treatment was

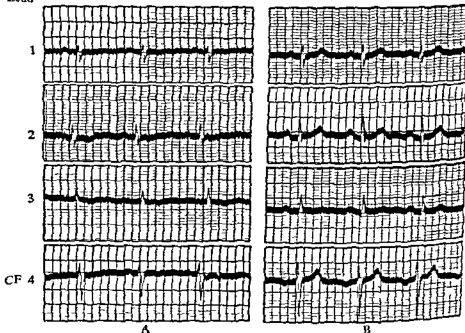


FIG 92 Electrocardiograms (four leads) in hypothyroidism (myxedema) male age 59 (*A*) before and (*B*) after thyroid therapy Basal metabolic rate at time of (*A*) = —46 per cent and at time of (*B*) = —17 per cent

found impracticable and given up However there has been recently a revival of the principle of therapy involved in the form of a medical thyroidectomy via irradiated iodine with prevention of any high degree of hypothyroidism by the administration of small doses of thyroid

Age The myxedema heart like myxedema itself has been found usually in middle age or later but it may occur in youth It is likely that a complication such as coronary heart disease coming independently or favored by the myxedema may help to account for the greater frequency of cardiac dilatation and weakness among the older victims of myxedema

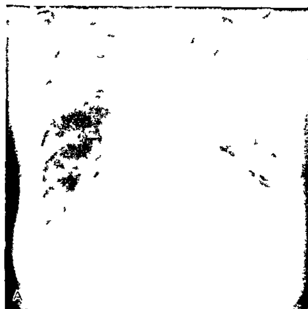




FIG 93 Roentgenograms showing great change in cardiac area (6 cm in the trans ve se diameter of the heart shadow) as the result of the successful treatment of myxe dema by thyroid administration Woman 66 years old

(*A*) Dec 5 1934 basal metabolic rate = —46 per cent

Cardiothoracic ratio in roentgenogram $= \frac{18\ 2}{24\ 0}$

(*B*) May 21 1935 basal metabolic rate = —13½ per cent

In this record the diaphragm is somewhat lower than in the former which exaggerates slightly the difference in size of the heart shadow

Cardiothoracic ratio $\frac{12\ 2}{23\ \text{-}}$

(Kindness of Dr J C Gant Madison College Tennessee)

Sex Sex has no particular relationship to the myxedema heart so far as we know

Other factors The most important factors controlling the incidence of the myxedema heart in any community are undoubtedly first the frequency of myxedema itself in that community, and second the ability of the medical profession to recognize and properly to treat it It undoubtedly is a preventable type of heart disease

Pathology An occasional finding in myxedema is considerable globular enlargement of the x ray heart shadow giving rise to the so-called myxedema heart The exact cause of such enlargement is not always clear and has been a subject of some controversy probably it is the result partly of dilatation partly perhaps of the increased bulk due to the myxedematous state affecting the heart tissues and certainly sometimes to an excess of fluid in the pericardium all three factors may play a role in increasing the area of percussion dullness or the roentgen ray heart shadow Functional regurgitation through the atrioventricular valves may occur with the dilatation but there is no endocarditis Pericarditis is not found despite the occasional discovery of large pericardial effusions the heart itself may show no actual enlargement in the midst of a large pericardial effusion Presenile arteriosclerosis especially involving the coronaries is reputed to be a general accompaniment of myxedema but convincing evidence of this is still lacking

Symptoms There are few symptoms of the heart involvement in myxedema the low level of activity in this condition probably preventing the cardiac dilatation and weakness from making themselves more evident Dyspnea has been noted in rare cases of congestive failure in myxedema and in a few patients with myxedema angina pectoris has occurred These symptoms occurring at the height of the endocrinopathy itself are sometimes cleared by thyroid therapy but sometimes induced or aggravated by the specific treatment which raises the metabolism and blood flow too rapidly coronary disease or other factors preventing the heart itself from keeping pace with the demands thus newly thrown upon it

Signs The only cardiovascular signs in the case of the myxedema heart are the occasional enlargement evident both on physical examination and by roentgen ray study (Figure 94) the sluggish heart action commonly observed in the same way and the constant finding of absence or inversion of the *T* wave in all leads of the electrocardiogram (Figure 93) This electrocardiographic sign is almost pathognomonic of myxedema and can be used along with the determination of the basal metabolic rate in following the progress of thyroid therapy There is frequently also a decrease in amplitude (low voltage) of the other complexes of the electrocardiogram the *P* and *QRS* waves which resume along with the *T* waves a more normal extent of excursion on treatment

The usual signs and symptoms of myxedema are generally obvious—slowed mental state dryness and thickening of hair and skin puffiness of subcutaneous tissue (myxedema) all over the body including the face weakness and dislike of cold The basal metabolic rate is generally reduced to 30 per cent below

the average normal or lower borderline cases with measurements of basal metabolic rate of minus 10 to minus 25 per cent are less likely to have heart trouble and usually these individuals have not true myxedema to start with

Also in myxedema a decrease has been found in the cardiac output circulatory velocity, peripheral flow, and total volume of blood

Course and prognosis The finding of evidence of significant cardiac involvement in myxedema is an important sign for it means that the grade of myxedema is a serious one or that other heart trouble such as coronary or hypertensive is present The discovery of cardiac enlargement is usually an incidental one in the course of routine examination but it should always be looked for and the cardiac response to the treatment of myxedema should be carefully followed Sudden death with or without angina pectoris may occur a few months or years after the finding of the myxedema heart Death postponed by careful thyroid therapy may come eventually from other complications without cardiac responsibility in fact a full length of life is possible under careful treatment Congestive failure as a cause of death in myxedema per se is very rare I myself have never seen a case

Complications Angina pectoris due to coronary disease is the most important complication of the myxedema heart especially after treatment of the myxedema has begun the elevation of metabolism by thyroid therapy may induce symptoms of coronary insufficiency Acute infections like pneumonia may appear as complications with serious prognosis General arteriosclerosis is common but not essential

Treatment. Digitalis has no definite beneficial influence on the cardiac enlargement or electrocardiographic abnormalities of myxedema Thyroid gland on the other hand has a striking effect clearing up these conditions more or less completely if given in sufficient dosage An amazing decrease in heart or pericardial size may sometimes be effected in four cases of Lerman Clark and Means series (1933) for example the transverse diameter of the heart shadow by teleroentgenogram decreased in the first case from 19 3 to 12 4 cm in six months in the second from 21 4 to 15 7 cm in six weeks in the third from 16 5 to 11 4 cm in eight and one half months and in the fourth from 19 4 to 15 5 cm in five months

Thyroid gland should be given very cautiously in the treatment of myxedema particularly when there is a history of angina pectoris for although marked general improvement may ensue and the heart resume practically normal size angina pectoris may be precipitated or increased by the raised level of metabolic rate and increased blood flow and sudden death may occur just when the myxedema itself is under control It may be necessary to give doses of thyroid so small that although the basal metabolic rate is not restored completely to normal angina pectoris is kept away or under partial control some myxedematous signs and symptoms may remain but life is prolonged A dose of ¼ to ½ gr (0 015 to 0 03 gm) of thyroid (U S P) daily may accomplish this instead of the usual larger doses (1 to 2 gr) Rarely the thyroid therapy banishes angina pectoris Digitalis should be given if there are in addition to the dilatation of the heart signs and symptoms of congestive failure

which do not yield to thyroid therapy alone but morphine is contraindicated

Differential diagnosis The myxedema heart must be differentiated from cardiac enlargement and weakness of other cause, from coronary heart disease and from infectious pericardial effusion This is usually readily done by the absence of cardiac symptoms of chronic valvular disease, and of hypertension by the typical electrocardiographic findings by the general signs of myxedema and by the response to thyroid therapy

DISEASES OF OTHER GLANDS

Parathyroid disease Little is to be said of the effect of parathyroid disease on the heart The decreased calcium content of the blood in tetany is associated with increase of the duration of cardiac systole, hyperparathyroidism and the administration of excessive amounts of parathormone cause by the increase of calcium content of blood an increase of calcium in the tissues likewise including the heart muscle We have no proof that these results are of any clinical significance

Pituitary disease The only association of abnormality of the heart with pituitary disease is the finding of cardiac enlargement (*hypertrophy*) especially of the left ventricle in acromegaly such enlargement may be great and out of proportion to the general splanchnomegaly found in this condition Whether it is the result of the somewhat increased basal metabolic rate in this disease or due to other factors is not known In one series of 24 patients marked heart failure was noted in 18 (75 per cent) six of this group died from that cause (Mason, 1936 1938) In gigantism the heart is not affected but bears a normal relationship to body size (Zondek 1920)

Basophilia of the posterior lobe of the pituitary gland has been noted in certain cases of pituitary adenoma with hypertension and in some patients with hyperpiesia and eclampsia (Cushing 1934) this finding has not been confirmed however as a characteristic occurrence in essential hypertension

Adrenal disease Adrenal disease has a direct effect on the heart as well as on the circulation Destruction of adrenal tissue (cortex) as in Addison s disease causes collapse marked hypotension and general muscular weakness including myocardial weakness but not structural heart disease The heart is smaller than normal both in volume and weight in part the result of the decreased amount of circulating blood and in part due to myocardial atrophy and the *T* waves of the electrocardiogram are depressed

Relief of the symptoms and signs of Addison s disease has been effected by adrenal plus sodium chloride therapy but the new specific therapy of adrenal insufficiency (Addison s disease) with desoxycorticosterone and cortisone must be followed with great care since serious cardiac enlargement and weakness may appear with toxic doses in fact measurement of heart size has been suggested as an objective check on large dosage of the hormone (McGavack 1942) it has been found that the dose of desoxycorticosterone acetate necessary to produce a given degree of cardiac enlargement varies inversely as the amount of sodium available in the tissues

Not only may dilatation of the heart result from excessive desoxycorticosterone therapy of Addison s disease but even high degrees of congestive failure along with changes in the electrocardiogram which recede or disappear when the drug is omitted The tendency to low voltage of the *QRS* and *T* waves found with Addison s disease is much exaggerated by excess of desoxycorticosterone (Currens and White 1944) These changes in the heart are probably due to or at least associated with a loss of body potassium Illustrations of the changes in the electrocardiogram and roentgen picture of the heart due to excessive desoxycorticosterone therapy are shown in Figure 94 on page 460

The stimulation that results from an adrenal medullary tumor (*pheochromocytoma*) can cause hypertension of paroxysmal nature which may be cured by removal of the tumor If the hypertension is sustained however removal of the tumor may have no effect on it splanchnic resection then being required The tumor may be located in tissue outside the adrenal glands themselves and then may be found with difficulty

Cortical adenomas of the adrenal may also play a role in hypertension they are more numerous than pheochromocytomas but their removal may not have any important effect on the hypertension present in such a case (Smithwick personal communication 1942)

Pancreatic disease *Diabetes mellitus* does not cause heart disease directly but it does favor arteriosclerosis and coronary artery disease (Root Bland Gordon and White 1939) At least 50 per cent of all diabetics die as a result of cardiovascular complications and the relative incidence of this cause of death is steadily increasing as other fatal complications are eliminated Marked atherosclerosis of the aorta with considerable dilatation is common Hypertension plays an important role in this group and frequently precedes the onset of the diabetes sometimes by several years Congestive failure due to hypertension or to coronary disease is not unusual but death comes most frequently from coronary occlusion (West 1935)

Excess of insulin does not apparently affect the heart seriously unless there is already heart disease the possible harmful effect from insulin shock (*hyper insulinemia*) however makes it advisable to use insulin cautiously in the presence of acute coronary thrombosis very severe angina pectoris and congestive failure Arrhythmias and electrocardiographic abnormalities following the use of insulin occur

Thymic disease Hypertrophy or persistence of the thymus gland is not attended by heart disease but is accompanied by general arterial hypoplasia The cause of the sudden death in the so-called status lymphaticus and its reputed relationship to the thymus gland are still unsolved mysteries The enlarged gland in child or adult is to be differentiated on physical examination and by roentgen ray from abnormalities of the great vessels

Genital glands Heart disease does not result from disease of ovaries or testes but functional disorders with cardiovascular symptoms of neurocirculatory asthenic type are commonly found especially at the time of the menopause in women or following double oophorectomy Hypertension of the essential type is also a frequent finding often but temporary at the time of

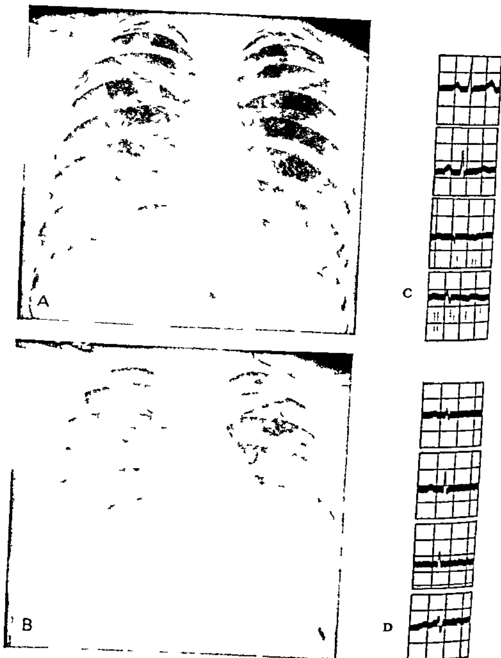


FIG 94 Roentgenograms and electrocardiograms in the case of a young woman with Addison's disease showing the toxic effect of excessive desoxycorticosterone acetate in treatment (*A*) Roentgenogram of the thorax Aug 13 1942 showing normal heart size and some prominence of the shadow of the pulmonary artery (*B*) Roentgenogram of the thorax Sept 9 1942 showing marked enlargement of the heart during the height of the effects from the desoxycorticosterone (*C*) Electrocardiogram more or less normal of this patient on Oct 24 1942 after the effects of the desoxycorticosterone had worn off (*D*) Electrocardiogram on Aug 30 1942 at the height of the toxic effect of the desoxycorticosterone

the menopause and this may affect the heart secondarily to cause hypertrophy Hamilton (1940) has not found however that the climacteric exerts any very severe strain on the heart of women already affected by heart disease A so-called fibroid heart has been said to result from uterine fibroid disease (fibroma) but there is no proof that such a condition exists, functional disturbances as noted above and premature beats undoubtedly accounting for this condition There has as yet been demonstrated no real myoma heart" (von Jaschke 1933) A change in the electrocardiogram consisting of a digitalis like depression of the *ST* segments and *T* waves, was noted by Scherf (1940) in some females with ovarian dysfunction and was cleared by estrogenic hormone therapy such changes are however rarely more than slight in degree and it is probable that some factor such as hyperventilation (see Chapter 9) secondary to the climacteric rather than the ovarian dysfunction itself is responsible

BIBLIOGRAPHY

THE HEART IN THYROID DISEASE AND IN DISEASES OF OTHER GLANDS OF INTERNAL SECRETION

Thyroid Disease Thyrotoxicosis

Barker P S Bohning, A. L and Wilson F N Auricular Fibrillation in Graves Disease *Am Heart J* 1932 VIII 121

Blumgart H L Freedberg A S and Buka P "Treatment of Euthyroid Cardiac Patients by Producing Myxedema with Radioactive Iodine" *Proc Soc Exper Biol & Med* 1948 LXVII 190

Blumgart H L Gargill S L and Gilligan, D R. "Studies on the Velocity of Blood Flow XIII The Circulatory Response to Thyrotoxicosis" *J Clin Investigation* 1930 IX, 69

Boas E. P "Cardiac Disorders Accompanying Exophthalmic Goiter Some Factors in Their Pathogenesis *J A M A* 1923 LXXX 1683

Bortin M M and Yohalem S B "Thyrotoxicosis Factitia Masked as Heart Disease" *Am Heart J* 1950 XXXIX 894

Coffen, T H "The Incidence of Heart Disease in the Pacific Northwest *Am Heart J* 1939 V 99

Ernstene A. C 'The Cardiovascular Complications of Hyperthyroidism *Am J M Sc* 1938 CXCI 248

Friedberg, C K and Sohval A R "The Occurrence and the Pathogenesis of Cardiac Hypertrophy in Graves Disease" *Am Heart J* 1937 XIII 599

Goodall J S "The Heart in Graves Disease *Practitioner* 1930 CV 37

Gordon E S and Albright E C "Treatment of Thyrotoxicosis with Radioactive Iodine." *J A M A* 1950 CXLIII 1129

Graybiel A and White P D Inversion of the T Wave in Lead I or II of the Electrocardiogram in Young Individuals with Neurocirculatory Asthenia, with Thyrotoxicosis in Relation to Certain Infections and Following Paroxysmal Ventricular Tachycardia" *Am Heart J* 1935 X 345

Greene A M and Hurxthal L M "A Postoperative Follow up Study of Four Hundred and Sixty Nine Thyrocardiac Patients" *New England J Med* 1941 CCXXV 811

Hamilton B E "Heart Failure of the Congestive Type Caused by Hyperthyroidism" *J A M A* 1924 LXXXIII 405

Hartwell A S Burrett, J B Graybiel, A and White P D "The Effect of Exercise and of Four Commonly Used Drugs on the Normal Human Electrocardiogram, with

Particular Reference to T Wave Changes *J Clin Investigation* 1942 XXI 409
Hurxthal L M Heart Failure and Hyperthyroidism with Special Reference to Etiology" *Am Heart J* 1928 IV 103
Jaffe H L and Ottoman R E "Evaluation of Radioiodine Test for Thyroid Function. *J A M A* 1950 CXLIII 515
Kepler E J and Barnes A R Congestive Heart Failure and Hypertrophy in Hyperthyroidism A Clinical and Pathological Study of 178 Fatal Cases *Am Heart J* 1932 VIII 102
Kocher A Ueber Morbus Basedow *Mitt am d Grenzgeb d Med u Chir* 1902 IX 1
Lahey F H End Results in Thyrocardiacs *Ann Surg* 1929 XC 750
Lerman J and Means J H Cardiovascular Symptomatology in Exophthalmic Goiter *Am Heart J* 1932 VIII 55
Lerman J and Salter W T "The Behaviour of Natural and Artificial Thyroid Protein. An Attempt at Biochemical Interpretation of the Effect of Iodine in Thyroid Disease *Tr Am A Study of Goiter* 1936 143
McEachern D and Rake G Study of Morbid Anatomy of Hearts from Patients Dying with Hyperthyroidism *Bull Johns Hopkins Hosp* 1931 XLVIII 273
Means J H *The Thyroid and Its Diseases* J B Lippincott Co Philadelphia 2nd ed 1948 (1st ed 1937)
Means J H and Richardson E P *The Diagnosis and Treatment of Diseases of the Thyroid* Oxford University Press New York 1929
Parade G W Relative Aorteninsuffizienz bei Morbus Basedow" *Deutsch med Wchnschr* 1935 LXI 1799
Rose E Ueber den Kropftod und die Radicalcur der Kropfe *Arch f klin Chir* 1878 XXII 1
Stewart H J and Evans W F "The Peripheral Blood Flow in Hyperthyroidism *Am Heart J* 1940 XX 715
Trousseau A "Exophthalmic Goitre" Lecture 58 on *Clinical Medicine* translated from the 3rd French edition (Paris 1867) by Sir John Rose Cormack and P Victor Bazire Lindsay & Blakiston Philadelphia 1873
Weller C V Wanstrom R C Gordon H and Bugher J C Cardiac Histopathology in Thyroid Disease Preliminary Report" *Am Heart J* 1932 VIII 8
White P D and Jones T D "Heart Disease and Disorders in New England" *Am Heart J* 1928 III 302
Wood J E Jr Jones T D and Kimbrough R D "The Etiology of Heart Disease Clinical Study of 623 Cases with Certain Observations on Race and Climate" *Am J M Sc* 1926 CLXXII 185

Myxedema and Cretinism

Blumgart H L Gargill S L and Gilligan D R "Studies on the Velocity of Blood Flow XIV The Circulation in Myxedema with a Comparison of the Velocity of Blood Flow in Myxedema and Thyrotoxicosis" *J Clin Investigation* 1930 IX 91
Burgess A M "Myxedema Controlled by Thyroid Extract for 52 Years" *Ann Int Med* 1946 XXV 146
Bustamante Marcaida R and Perez Stable Carreno E "Derrame pericardico en el corazón mixedematoso *Rev cubana de cardiol* 1949 X 205
Fahr G "Myxedema Heart" *J A M A* 1925 LXXXIV 345 *Am Heart J* 1927 III 14 and 1932 VIII 91
Fournier J C M "The Circulatory Apparatus in Myxedema" *Proc Staff Meet Mayo Clin* 1942 XVII 212
Kern R A Soloff L A Snape W J and Bello C T "Pericardial Effusion A Constant Early and Major Factor in Myxedema Heart" *Tr A Am Physicians* 1948 LXI 158 *Am J M Sc* 1949 CCXVII 609
Lerman J Clark R J and Means J H "The Heart in Myxedema Electrocardiograms and Roentgen Ray Measurements Before and After Therapy" *Ann Int Med* 1933 VI 1251
Paddock F K "Massive Ascites Due to Myxedema Report of a Case *New England J Med* 1950 CCXLII 872

Thacher C "The Electrocardiogram in Cretinism and in Mongolian Idiocy" *Am J Dis Child* 1924 XXVIII 25
Thacher C and White P D "The Electrocardiogram in Myxedema" *Am J M Sc* 1926 CLXXI 61
Zondek H Das Myxodemherz" *Munch med Wchnschr* 1918 LXV 1180 *ibid* 1919 LXVI 681

Other Endocrine Disorders

Courville C B and Mason V R "The Heart in Acromegaly" *Arch Int Med* 1938 LXI 704
Currens J and White P D Congestive Heart Failure and Electrocardiographic Abnormalities Resulting from Excessive Desoxycorticosterone Acetate Therapy in the Treatment of Addison s Disease *Am Heart J* 1944 XXVIII 611
Cushing H "Hyperactivation of the Neurohypophysis a the Pathological Basis of Eclampsia and Other Hypertensive States *Am J Path* 1934 X 145
Hamilton, B E The Influence of the Climacteric on the Course of Organic Heart Disease" *Proc New England Heart A* 1940-41 p 29
Hench P S Kendall E C Slocumb C H and Polley H F "The Effect of a Hormone of the Adrenal Cortex (17 Hydroxy 11 Dehydrocorticosterone Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis Preliminary Report" *Proc Staff Meet Mayo Clin* 1949 XXIV 181
Hejtmancik M R et al Acromegaly and the Heart *Ann Int Med* 1951 XXXIV 1445
Holler J W "Potassium Deficiency Occurring During the Treatment of Diabetic Acidosis" *J A M A* 1946 CXXXI 1186
Kyle L H and Knop C Q "Simulation of Cardiac Disease by Adrenocortical Failure in Infant" *New England J Med* 1950 CCXLIII 681
Lisa, J R et al "Arteriosclerosis with Diabetes Mellitus A Study of the Pathologic Findings in 193 Diabetic and 2 250 Non Diabetic Patients" *J A M A* 194_ CXX 192
McGavack T H "The Size of the Heart as a Guide to the Treatment of Addison s Disease with Desoxycorticosterone Acetate *Am Heart J* 194_ XXIV 99 and 1944 XXVII 331
Martin H E and Wertman M "Electrolyte Changes and the Electrocardiogram in Diabetic Acidosis" *Am Heart J* 1947 XXXIV 646
Mason V R "The Heart in Acromegaly *Tr A Am Physicians* 1936 LI 220
Nadler C S Bellet, S and Lanning M "Influence of the Serum Potassium and Other Electrolytes on the Electrocardiogram in Diabetic Acidosis *Am J Med* 1949 V 838
Neubauer R A and Frelick R W "Spontaneous Hyperpotassemia as a Cause of Death in Diabetic Acidosis" *Am Heart J* 1950 XL 793
Raab W "Cardiovascular Effects of Desoxycorticosterone Acetate in Man *Am Heart J* 1942 XXIV 365
Root, H F Bland E F Cordon W H and White P D "Coronary Arteriosclerosis in Diabetes Mellitus A Postmortem Study *J A M A* 1939 CXIII 27
Sacks H A Crisis in Addison s Disease Simulating Coronary Thrombosis" *Illinois M J* 1937 LXXI 475
Scherf D The Respiratory and the Circulatory System in Females with Ovarian Dysfunction" *Ann Int Med* 1940 XIII 1414
Somerville W et al "Electrocardiogram in Addison s Disease" *Medicine* 1951 XXX 43
Thorn G W Dorrance S S and Day E Addison s Disease Evaluation of Synthetic Desoxycorticosterone Acetate Therapy in 158 Patients" *Ann Int Med* 194_ XVI 1053
Thorn G W Nelson K R and Thorn D W "Study of Mechanism of Edema Associated with Menstruation" *Endocrinology* 1938 XXII 155
von Jaschke R T Der Zirkulationsapparat beim Myom *Arch f Gyn* 1933 CLV 6
West H F "Diabetes and Cardiovascular Disease *Mod Concepts Cardiovas D s* 1935 IV No 1
Zondek H "Herzbefunde bei endokrinen Erkrankungen" *Deutsch med Wchnschr* 1920 XLVI 1239

CHAPTER 19

HYPERTENSIVE HEART DISEASE
ESSENTIAL HYPERTENSION
HYPOTENSION

HYPERTENSIVE HEART DISEASE

Introduction Since the last revision of this book seven years ago there have been innumerable studies and published reports concerning hypertension and hypertensive cardiovascular disease many of them of considerable interest and value, as may be observed on perusal of the additions of references to representative publications in the Bibliography at the end of the chapter Nevertheless the mechanism of the so-called essential type of hypertension still eludes us *another few years may very well reveal to us the answer,* or the answers since so many able workers are engaged on the problem Meanwhile to date distinct advances in therapy, though empirical have been scored

The most common and important of all types of heart disease by and large the world over is that due to systemic hypertension with elevation of the *diastolic* blood pressure It is often serious and frequently followed by congestive failure and death It has been estimated that nearly 100 000 people die annually in the United States (population of about 130 000 000) as the result of heart failure due to hypertension and that 7 000 more die from other consequences of high blood pressure In a series of 30 265 autopsies with 4 678 cardiovascular deaths (15 45 per cent) 2 597 were hypertensive cases (55 5 per cent of the cardiovascular deaths and 8 6 per cent of the total autopsies) the chief factor responsible for the hypertensive deaths was cardiac (2 059 cases or 79 per cent divided into the group with myocardial insufficiency—congestive heart failure—with 1 124 cases or 43 per cent and that with coronary fatalities with 935 cases or 36 per cent) while cerebral hemorrhage caused death in 362 patients (14 per cent) and renal insufficiency in 176 cases (7 per cent) (Clawson 1941) In New England systemic hypertension is a primary or a secondary factor in at least 30 per cent of cases of heart disease Until the last decade or two the condition had a variety of other names or was missed entirely unless blood pressure studies revealed the hypertension It has made up a considerable percentage of cases of so-called cardiorenal disease , of so-called myocarditis and of cardiac enlargement

Heart disease due to pulmonary hypertension is much less common than that due to systemic hypertension but it is of considerable interest and importance and will be discussed in the next chapter Hypertension in the portal circulation will be taken up in connection with diseases of the blood vessels in Chapter 28 Venous hypertension is discussed in Chapter 6 under Venous Blood Pressure and in Chapter 30 on Congestive Heart Failure

Etiology *Cause* The cause of the heart disease is known—high blood pressure often abetted by some other factor especially coronary disease The fundamental cause of the high blood pressure in the majority of cases has been however obscure and not associated with any constant clinical findings hence it has been called essential or primary The term hyperpiesia (ὑπερ over and πιεζειν to press) has also been applied to it and another synonym is vascular or arterial hypertension indicating that the blood vessels are responsible

Innumerable theories as to the cause of hypertension have been advanced since its discovery over a generation ago and some of these theories have now become facts in other words there are at least several different causes although that of the bulk of the cases (those with essential hypertension) is still (1951) to be elucidated The association of heart disease with kidney disease was demonstrated by Bright more than a century ago (1836) but the mechanism of such association was of course unknown Gull and Sutton (1872) pointed out the arteriolar fibrosis found in Bright s disease and in our own generation the vascular factor in hypertension has had the limelight During the last decades however attention has been directed again to the kidneys by the pioneer work of Goldblatt (1934) who demonstrated that hypertension can be produced in animals by obstructing by a clamp the blood flow through a renal artery and by the finding of pressor substances called angiotonin and hypertensin produced by the kidney with their neutralization by other (antipressor) substances (Tigerstedt and Bergmann 1898 Houssay Fasciolo and Taquini 1938 Page and his associates 1940 1941 Harrison Grollman and Williams 1940) Suffice it to say that the most acceptable and widely held theory in the light of our present knowledge is that the arterioles more or less universally throughout the body have through some direct toxic or nervous influence become irritable and pass into a state of vasoconstriction thereby increasing the resistance to the circulation of blood to which the heart responds with a resulting rise of arterial blood pressure It is possible that the renal arterioles may play the major role in this process At first this type of hypertension is slight and transient and may largely escape notice Its later course is very variable the *arteriolar spasm* may subside with a spontaneous cure of the hypertension it may increase and become fixed as in the ordinary well recognized case or it may progress to an extreme and rapid degree giving rise to the so-called malignant hypertension According to this theory there are at first no (as yet) recognizable pathologic changes arteriolar sclerosis arterial sclerosis renal damage (arteriosclerotic nephritis) and cardiac enlargement are secondary effects of long sustained hyperpiesia in

time the *arteriolar sclerosis itself* may be responsible for at least some of the hypertension and prevent its reduction

Hypertension is in some cases (a distinct minority) secondary to an easily discoverable cause such as gross nephritis polycystic kidneys adrenal tumor increased intracranial pressure, or congenital coarctation of the aorta or is temporarily induced by urinary obstruction congestive heart failure coronary insufficiency, pain exertion or excitement or concussion of the brain, frequently slight systolic hypertension attends thyrotoxicosis complete heart block and aortic regurgitation or marked sclerosis Under such circumstances the hypertension is not called essential or hyperpiesia In the case of hypertension of renal origin there may be an added toxic effect from renal insufficiency with or without definite uremia The surgical kidney as such is not however commonly a cause of hypertension

A number of practical classifications of hypertension have been proposed in the past a good example of which presented by Gilchrist (1941) was published in the third edition of this book A recent system, bringing this subject up to date has been presented by Page (1949) This is reproduced below It is to be observed that diastolic hypertension is far more important than systolic hypertension systolic hypertension with normal or only very slightly elevated diastolic blood pressure is much less important clinically and is apparently in the main the result of arteriosclerosis

Table 8

CLASSIFICATION OF HYPERTENSION (PAGE)

Clinical	*Experimental*
I Nervous Participation	
Poliomyelitis of brain stem	Cerebral ischemia
Porphyria	Cushing s experiment
Increased intracranial pressure	Resection of sinus and aortic depressor nerves
Sclerosis of carotid sinus	
Resection of glossopharyngeal nerve	Hypertension from audiogenic stimulus
Emotion	
Tabes dorsalis	
II Cardiovascular Participation	
Coarctation of aorta	Clamping of aorta above renal vessels
Heart failure	
Arteriovenous fistula	
Arteriosclerosis	
III Endocrine Participation	
Hypophysis—basophil adenoma	Anterior lobectomy diminishing blood pressure
Adrenals—pheochromocytoma	
Cortical carcinoma	Adrenaline hypertension
Cortical hyperplasia	Desoxycorticosterone acetate *hypertension*
Thymus—*carcinoma with Cushing s* syndrome	Bilateral adrenalectomy abolishes hypertension
Placenta—associated with toxemia of pregnancy	Cerebrum (1951)

IV Renal Participation

Glomerulonephritis	Antikidney serum nephritis
Obstruction to renal vessels	Mechanical constriction of renal arteries or veins
Pyelonephritis	Mechanical compression of ureters
Prostatic obstruction	Cellophane or silk perinephritis
Polycystic kidneys	
Crush syndrome	
Periarteritis nodosa	
Perinephric constriction of the parenchyma	

Hyperpiesia (essential hypertension) accounts for fully 95 per cent of the cases of hypertensive heart disease and obvious renal disease for most of the rest About two thirds of the cases of established diastolic hypertension show cardiac enlargement on examination Still others have lesser grades of enlargement too slight to discover clinically hypertension whether or not of the essential type may be too slight or recent in onset to cause any cardiac hypertrophy at all

Age Hypertensive heart disease like hypertension itself (especially hyperpiesia) is commonest in middle age and after signs of it appear on the average ten years after the onset of sustained hypertension of an important degree except when there are complications (valvular disease or coronary disease) to make its effect more quickly evident Of a series of 708 cases of hypertensive heart disease 62 per cent were in the sixth and seventh decades (29 per cent in the sixth and 33 per cent in the seventh) 17 per cent were over seventy years of age 16 per cent were in the fifth decade 4 per cent in the fourth 1 per cent in the third and 0 5 per cent were below twenty years old thus only 21 per cent of the cases were less than fifty years of age (White and Jones 1928) In a more recent series of 1 249 cases 68 per cent were between fifty and seventy (White 1936) The youngest case of essential hypertension with autopsy on record that I know about has been reported by Taussig and Remsen (1935) a colored boy two years old

Sex There is not much difference between the sexes in the incidence of hypertensive heart disease In White and Jones series of 708 cases 55 per cent were female and 45 per cent male In the more recent series of 1 249 cases from my own practice 51 per cent were male and 49 per cent female Hypertension itself on the other hand is far more common in females than in males by a ratio of about 2 to 1 Yet it is true that it is much more serious in the male Blackford and Wilkinson (1932) found the mortality rate after ten years twice greater in men and among 50 consecutive cases of my own with serious cardiovascular sequelae of hypertension selected for sympathectomy 38 were male and 12 were female (White et al 1950)

Heredity Of all known etiologic factors in the production of hypertension and so of hypertensive heart disease heredity ranks as of the greatest importance Frequently many members of one family in the course of a few

generations have either shown essential hypertension or have had troubles coming from such a condition The way in which heredity acts is obscure but we do know of its great significance

Race and *climate* are factors of some importance Hypertension is less marked in tropical and semitropical climates and it is said to be uncommon in certain nationalities like the Chinese when in their own country whether this is because of race or of other factors like tempo of life or diet we do not know It is especially common among the Negroes in the United States apparently twice as common as in the white population for reasons unknown it is said that in Africa on the other hand hypertension is rare among the Negroes who tend however to succumb to other ills especially tropical diseases at relatively early ages before the years when essential hypertension is at its peak in America We need much international research on this problem

Diet and obesity Overeating and obesity frequently are associated with hypertension and hypertensive heart disease but the relationship is a very inconstant one on both sides A high protein diet was once blamed for the production of hypertension but this has been refuted, on the other hand a diet overrich in food value in general may be of importance During the war in Holland over a period of starvation from September 1944 to May 1945 there was a frequent lowering of blood pressure associated with weight loss especially in hypertensive patients (Lups and Francke 1947) There are problems here in need of solution

Nervous and physical strain It is believed by many observers that a life of high nervous tension favors the production of hyperpiesia or at least its aggravation the latter is the more likely Physical strain and constant laborious work although sometimes blamed as aggravating factors have been largely exonerated in late years indeed it seems possible that physical exercise in moderation at least may protect against hyperpiesia

Endocrine disturbances are frequently attended by hypertension but rarely by marked hypertension these disturbances are especially associated with the ovarian function (for example, menopause and oophorectomy), with thyrotoxicosis and with adrenal or pituitary tumors In the case of thyroid or adrenal or pituitary oversecretion surgical removal of a large part of the thyroid gland or of an adrenal or pituitary tumor may result in a return of blood pressure to normal The discovery that an excess of basophilic cells is present in the posterior lobe of the pituitary gland (hypophysis) in certain cases of pituitary adenoma with hypertension and of eclampsia (Cushing 1932) suggested that hyperpiesia might have its basis therein but this suggestion has not been confirmed only a small minority of cases are to be so explained

Infections and poisons have not been shown to have any close connection with the pathogenesis of hyperpiesia this statement includes lead long blamed for hypertension

Pathology The pathology of hypertensive heart disease is as a rule very

simple Both cardiac and vascular abnormalities in chronic hypertension are primarily but natural responses of muscle to increased work Hypertrophy of the individual muscle fibers of the left ventricle is always present sometimes to such a degree that the heart is greatly enlarged (Figure 95) A heart weight of about 500 gm (normal = 200 to 350 gm) is common and in rare cases this may be increased to 750 or even to 1 000 gm With the development of failure

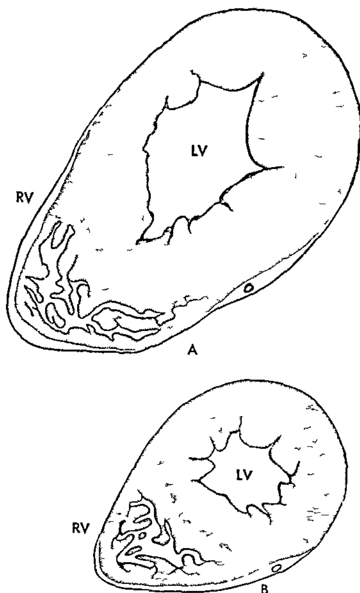


FIG 95 Drawings showing cross sections (actual size) of (*A*) an enlarged hypertensive heart and of (*B*) a normal heart at a level two thirds of the distance from base to apex of the ventricles LV = left ventricle RV = right ventricle

dilatation appears changing the appearance of left ventricular hypertrophy from concentric to eccentric Such left ventricular dilatation is followed by dilatation of the mitral valve ring functional mitral regurgitation dilatation of the left atrium and enlargement of the right ventricle and atrium too if the left ventricular failure lasts long enough It has been suggested that the primary hypertrophy of the heart muscle begins only after it has been strained or traumatized and somewhat dilated by the early efforts to overcome the effect of the arteriolar constriction Since with systemic hypertension the pulmonary arterial blood pressure usually remains normal (until the left ventricle fails) the right ventricle is unaffected early in the disease Eventually after the left ventricle has begun to fail the pulmonary blood pressure rises and the right ventricle in its turn is subjected to considerable strain and begins to enlarge as a matter of fact the commonest cause of right ventricular enlargement is failure of the left ventricle secondary to systemic hypertension

There is no actual myocarditis or myocardial degeneration in most cases of uncomplicated hypertensive heart disease even in massive hearts with marked congestive failure, some myocardial scarring (fibrosis usually in small areas) is however not uncommon even in the absence of coronary disease (Levine V 1934) Endocarditis and pericarditis do not occur primarily in this type of heart disease although endocardial sclerosis most marked in the left atrium which first bears the brunt of left ventricular failure was found in all of a series of 27 hypertensive hearts (Levine V 1934)

The aorta normal at first becomes dilated in older and chronic cases but never to the degree observed in advanced syphilitic aortitis Some of the dilatation seen by roentgen ray examination is not found post mortem since it is temporary depending on the intra aortic hydrodynamic state The vascular dilatation may extend a little into the aortic branches especially into the innominate and carotid arteries Rarely the aortic media may split to cause a dissecting aneurysm when hypertension is complicated by an abnormally weak spot in the aortic wall

Thickening of the arteries and arterioles throughout the body is a common finding in chronic hypertension and in all probability is a vascular response to the hypertension Arteriolar sclerosis and obliteration may complicate the picture Hypertension without arteriosclerosis and arteriosclerosis without hypertension are frequent findings but the two combined are as frequent as either condition alone Renal arteriolar sclerosis is preponderant and is universally found in the higher grades of hypertension although not as a rule at the onset of the disease

Symptoms There are no symptoms of hypertensive heart disease until complications arise the condition is often discovered incidentally in the course of routine examination Usually the person feels perfectly well and is simply annoyed by the discovery of the high blood pressure or of the enlargement of the heart Occasionally however, there are headaches and a coincident neurocirculatory asthenia with its various symptoms including palpitation heartache and dyspnea These symptoms are frequently erroneously attributed

by patient and doctor alike either to the high blood pressure or to heart disease although it is true that a person subject to neurocirculatory asthenia will have more symptoms if the blood pressure is high and the heart is enlarged than when the blood pressure and heart are normal and in some cases headache is part of a disturbance of the cerebral circulation incident to the hypertension (hypertensive encephalopathy) A neurosis is common with hypertension and hypertensive heart disease usually the result of fear of the high blood pressure When true symptoms of hypertensive heart disease do arise they are most commonly those of cardiac insufficiency which may increase to well marked congestive failure resulting from the myocardial strain and fatigue which involve primarily the left ventricle

Dyspnea on exertion is usually the first authentic symptom tending to increase in degree unless checked by the institution of proper treatment With marked failure dyspnea may become constant and prevent a recumbent position (orthopnea) Or there may be sudden attacks of acute failure of the left ventricle occurring during sleep at night or less often in the daytime after exertion or excitement with engorgement of the pulmonary circulation pulmonary edema and sometimes the setting off of asthmatic respiration Such an attack of wheezing is called cardiac asthma and is not an infrequent syndrome in the case of the failing hypertensive heart it varies considerably in duration but lasts usually about an hour

Pain is less common in hypertensive heart disease than is dyspnea It takes two forms sometimes a precordial ache due to an associated neurocirculatory asthenia (or effort syndrome) aggravated by the cardiac enlargement and sometimes angina pectoris from an associated coronary disease or syphilitic aortitis Angina pectoris however though common in hypertension because of the age incidence is not so characteristic as is dyspnea for the hypertensive strain results in an inability of the left ventricle to maintain the general circulation more often than in the inability of the coronary circulation to supply the heart muscle with blood unless we accept the possible theory that some hypertension especially if it involves the diastolic pressure may result from the need of greater force to maintain an adequate coronary circulation The prolonged pain of coronary occlusion occasionally complicates hypertensive heart disease

Palpitation is common in hypertension with or without heart disease especially in sensitive persons due either to the consciousness of the forceful heart action with normal rhythm particularly on exertion or excitement or to the occurrence of unimportant premature beats paroxysms of tachycardia or atrial fibrillation These various disturbances of rhythm are common in hypertensive heart disease but they are not characteristic Of the group of 708 cases of hypertensive heart disease of White and Jones (1928) 92 (or 13 per cent) had atrial fibrillation (14 of these were paroxysmal in type) paroxysmal tachycardia was noted in 11 patients (1 5 per cent) atrial flutter in 2 (0 3 per cent) and atrioventricular block in 13 (1 8 per cent)—the last named being due to an associated coronary disease and not to the hypertension

Other symptoms frequently found in essential or in nephritic hypertension with or without heart disease are familiar tinnitus weakness nosebleeds or other hemorrhages symptoms of cerebral accident (aphasia and paralysis) whether transient (hypertensive cerebral vascular crises or minute lesions) or *more or less lasting (cerebral hemorrhage or thrombosis)*, and symptoms of renal insufficiency (drowsiness coma and vomiting from uremia) The term hypertensive encephalopathy is used to cover all the various cerebral vascular disturbances due to hypertension from slight dizziness to extensive apoplexy, in frequency as a serious complication it ranks below the cardiac effects but above the renal

Signs The only constant sign of hypertensive heart disease is cardiac enlargement due mainly to left ventricular hypertrophy The hypertension itself responsible for this enlargement may have subsided at the time of examination though some trace of it usually exists If there is no increase in heart size even though hypertension is present we cannot label the condition hypertensive heart disease although as after rheumatic fever we may speak of potential heart disease In the early stages of hyperpiesia and even in more chronic cases when the blood pressure is but slightly elevated the heart may be able to stand the strain without increase in size but a normal heart size is rare if it exists at all, with markedly high blood pressure of long duration Finally it is to be observed that the cardiac enlargement of hypertensive heart disease may be present in slight degree to be discovered only at postmortem examination not being sufficient to give evidence during life An addition to the heart weight of 25 50 or perhaps even 100 gm in the absence of dilatation can probably not be detected clinically even by careful roentgen ray examination unless there are frequent serial records Hence the clinical statistical report that about two thirds of the cases with hypertension eventually show cardiac enlargement undoubtedly falls somewhat short of the actual figure as indicated by the statistical study of Murphy and his associates (1932) who found that in a series of 375 cases of essential (primary) hypertension examined post mortem the heart weights were 400 gm or above in 81 87 per cent (normal upper limit of heart weight = 350 gm in the male and 300 gm in the female)

In systemic hypertension with or without heart disease the aortic second heart sound is usually accentuated sometimes to a striking degree When the left ventricle begins to fail the pulmonary second heart sound increases *in intensity in its turn as the pulmonary blood pressure rises and finally* the pulmonary second sound equals or quite commonly exceeds the aortic second sound in intensity even though the latter continues to be louder than normal The changing relationships of the intensities of these two sounds is of great interest and importance affording a valuable but much neglected clue to the degree of sufficiency of the left ventricle

With increasing size of heart and the development of dilatation of left ventricle and aorta under the strain of the hypertension apical and aortic systolic murmurs appear and are common in the more advanced cases the former due to functional mitral insufficiency and the latter chiefly to the aortic dilata

tion In still more advanced cases especially when arteriosclerosis complicates the picture the aortic valve ring itself may stretch either temporarily under the head of pressure or more or less permanently to give rise to an aortic diastolic murmur (aortic regurgitation usually functional) In a series of 500 cases of hypertension (Paullin 1927) a mitral systolic murmur was noted in 26 per cent an aortic systolic murmur in 6 per cent and an aortic diastolic murmur in 2½ per cent in another series of 200 consecutive autopsied cases of hypertensive heart disease with normal aortic valves reported by Garvin (1940) a diastolic murmur had been heard at the base of the heart apparently aortic in origin in 14 cases resulting in a frank error in etiologic diagnosis in four instances

The aortic dilatation due to hypertension may not be marked enough to be found on physical examination but it is generally easily seen fluoroscopically It consists of a general enlargement of the whole thoracic aorta The ascending aorta is not as a rule so dilated as in syphilitic aortitis and there are no aneurysmal pouches A point of especial interest concerning the aortic dilatation in hypertension and incidentally also in cases of aortic regurgitation is that the dilatation is at first functional or dynamic at that stage failing to appear at autopsy even though very evident by roentgen ray examination during life

A common sign resulting from two factors the vascular dilatation and the pushing up of the great vessels by the cardiac enlargement and the high diaphragm so often found in obese persons especially women with hypertension is a prominence with pulsation of the innominate artery and the origin of the carotid artery at the base of the right side of the neck just above the inner end of the clavicle this is so marked sometimes that it resembles a small aneurysm

When congestive heart failure arrhythmias or other complications arise the usual signs of such troubles appear and the heart tends in the case of failure to become very large with increasing dilatation The appearance of gallop rhythm of the protodiastolic type is a frequent and serious sign of cardiac dilatation and failure in hypertensive heart disease The relative frequency of arrhythmias in hypertensive heart disease has been noted above their incidence is less in hypertension as a whole One of the most important disorders of heart action—pulsus alternans (see Chapter 8)—is relatively common in the case of the failing hypertensive heart and is much more common than generally thought it is most readily detected during the course of blood pressure measurement and it usually means that death is at best but a few years off (see Chapter 30)

One of the most helpful and constant signs of chronic hypertension and therefore usually associated with hypertensive heart disease is sclerosis of the arteries in the eye grounds (fundi oculorum) this is far more constant than in the case of general or coronary arteriosclerosis or of nephritis In slight to moderate grades of hypertension there may be little change in the fundi from none at all to silver wire appearance of the arterioles with nicking of the veins where the arteries cross them but in advanced or serious cases

hemorrhages appear in the eye grounds and areas of degeneration are found (see Figure 9 page 54) Moreover an early finding of marked retinal changes suggests that the type of hypertension is malignant" with a bad prognosis (even though the kidneys may be relatively normal at the time)

Signs of serious involvement of the brain may appear in the course of hyper tensive heart disease such as paralyses and abnormal reflexes or there may develop evidence of involvement of the kidneys albuminuria many casts in the urinary sediment oliguria low specific gravity of urine lowered renal function and nitrogen retention in the blood but it is to be remembered that in congestive heart failure due to hypertension albuminuria casts and other urinary abnormalities may be caused by congestion without nephritis and that a relatively unimportant vascular nephritis may develop secondarily due to the hypertension with such signs as those noted above and without con gestive failure

The blood pressure in hypertensive heart disease generally remains high but sometimes either because of spontaneous remission or because of heart failure or general vasomotor collapse and in some cases evidently aided by treatment it may fall to average normal or nearly normal levels leaving ob scure the cause of the cardiac enlargement and failure unless knowledge exists of the previous hypertension The diastolic pressure in such cases may be maintained at a somewhat high level (100 to 110 mm for example) even though the systolic pressure has fallen to 150 mm or below this relatively high diastolic pressure and low pulse pressure may in some cases reveal the pre vious hypertension In fact as already noted in the discussion of the clinical classification of hypertension the systolic level of the blood pressure is far less important than the diastolic so far as strain on heart arteries and kidneys is concerned a rise of a few millimeters of mercury of diastolic pressure is a great deal more serious than several times that rise of systolic pressure A full pulse pressure with elevated systolic pressure and normal diastolic is common in advanced sclerosis of the larger arteries (with loss of elasticity) and rela tively normal arteriolar circulation (that is, without essential hypertension)

It is not known how frequently cardiac enlargement is the result of an old hyperpiesia in the absence of hypertension at the time of examination and without evidence of valvular disease serious coronary disease pulmonary fibrosis or pericardial disease Some writers believe that it is always or almost always so produced This is a possibility but by no means a certainty Some causes for enlargement of the heart exist which are not yet clear while others previously unrecognized have in recent years been brought to light More study of this problem is needed

The systolic pressure in established hypertension varies from 150 to over 300 mm of mercury it is usually about 200 The diastolic pressure varies from 90 to 180 but is usually 110 to 120 The pressure readings (especially the systolic) vary greatly among different individuals and on different occa sions in the same individual Repeated measurements must often be made before the customary basal blood pressure levels for a given patient are dis

covered uninfluenced by excitement exertion or fatigue It has been found as would be expected that the blood pressure levels recorded by the patient himself or herself at home tend to be distinctly lower than they are in the clinic or doctor s office (Ayman and Goldshine 1941) It must be remem bered however that neither record is truly representative and that hypertension until fixed is likely to go through wide swings from day to day or hour to hour The lability of the pressure is of some importance in prognosis and treatment too the more favorable cases tending more often to show pressures close to normal To test the degree of the lability various procedures have been introduced including especially (1) the *measurement* of the blood pressure *at frequent intervals* day and night (2) the *cold pressor test* consisting of immersing one hand in ice cold water at 40 F for 30 to 60 seconds which will cause a mean rise of over 30 mm of mercury in systolic pressure and of over 25 mm in diastolic pressure in hypertensive individuals or somewhat less in hyperreactors (who may some day become hypertensive) and much less in normal nonhypertensive persons (Hines and Brown 1936) (3) the *sedation test* consisting of the effect of extreme sedation by the ingestion of 3 gr of Sodium Amytal every hour for three doses the blood pressure dropping to normal in the early or mild and labile cases and (4) the *postural test* the diastolic pressure rising in hypertensive cases 15 to 30 mm with less change in the systolic level and hence a drop in pulse pressure readings on assuming the erect position

A very high diastolic pressure is a bad sign and a constant finding of such a pressure over 130 mm of mercury means that without special treatment but a few months or years of life remain The auscultatory gap found by the auscultatory method of sphygmonanometry (discussed in Chapter 6) and pulsus alternans (to be discussed in Chapter 30) are both common in hyper tension and appear during blood pressure studies The blood pressure should be measured in spite of the presence of atrial fibrillation an approximate figure so obtained is generally sufficiently accurate When hypertensive crises occur due to adrenal medullary tumors (pheochromocytomata) or to vasomotor (arteriolar constriction) storms in the course of chronic hypertension sometimes with serious effects such as apoplexy the blood pressure may sud denly rise 50 to 100 or more millimeters systolic and half that diastolic

Special tests for a *pheochromocytoma* have been developed consisting of sharp increase of blood pressure on administration of histamine Mecholyl or tetraethylammonium chloride no reaction to epinephrine and reduction of blood pressure on intravenous injection of benzodioxane The more established tests are those with histamine (Roth and Kvale 1945) and benzodioxane (Goldenberg Snyder Aranow 1947) The former test consists of determin ing the basal blood pressure and pulse records after recumbency for ½ to 1 hour then every minute for 15 minutes after the intravenous injection of 0 025 to 0 05 mg of histamine (0 25 to 0 5 cc of 0 01 per cent solution in normal saline) a positive reaction is shown by a sharp rise of blood pres sure of 100 mm or more in the presence of a pheochromocytoma in contrast

to a much slighter rise in a case of essential hypertension The severity of this reaction has resulted generally (except when the blood pressure is not much elevated to start with) in replacement by the benzodioxane test, which consists of the intravenous injection in 2 minutes via a normal saline drip (in operation for 20 to 30 minutes before the test) of 0 25 mg per kilogram body weight in 1 per cent solution of piperidymethyl benzodioxane (933 F) an adrenolytic or epinephrine antagonistic substance a positive reaction *consists of a considerable fall in both systolic and diastolic pressures in the* course of a few minutes Less satisfactory testing for a pheochromocytoma includes perirenal air insufflation which can be difficult and dangerous and nondiagnostic in some cases when the tumor is situated not at the adrenal gland but elsewhere along the sympathetic chain as it sometimes is

Roentgen ray examination in hypertensive heart disease shows cardiac enlargement chiefly of left ventricular type (Figure 96 illustration below) and



FIG 96 Roentgenogram showing a moderately enlarged hypertensive heart with prominence of the left ventricle The arc of the descending aorta is well seen above the heart shadow because of its increased density (arteriosclerosis) The pulmonary artery is not enlarged there has been no pulmonary vascular congestion

general dilatation of the aorta with prominence of both ascending and descending portions in the thorax Later in the disease when left ventricular failure begins greater cardiac enlargement is found due to dilatation and to involvement of the right side of the heart and of the left atrium then the lung hilus shadows and the pulmonary artery shadow tend also to be prominent in keeping with the newly developed hypertension in the pulmonary circulation

Electrocardiography often shows no abnormality in hypertensive heart disease but in the majority of chronic cases there is characteristic hypertensive pattern (Figure 97A) consisting of lowering to inversion of the *T* waves in Lead 1 and in the leads over the left ventricle (V_4 V and V_6) and of in

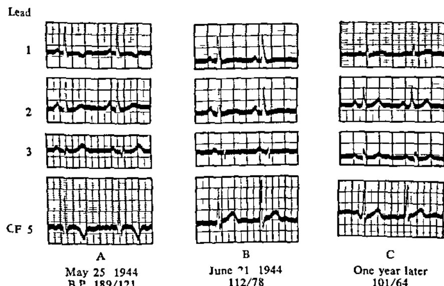


FIG 97 Reversal of the hypertensive electrocardiographic pattern after lumbodorsal sympathectomy Male age 39 Lumbodorsal sympathectomy right side May 31 1944 left side June 9 1944

creased amplitude of the *R* waves in these same leads there is frequently also left axis deviation as found in the classical bipolar limb leads although a horizontal heart position commonly found in hypertensive patients is more responsible for such axis deviation than is left ventricular enlargement It is likely that dilatation in addition to hypertrophy of the left ventricle is responsible for this abnormality of the electrocardiogram as borne out by the return to a more normal record in some cases when the hypertension and left ventricular strain therefrom are relieved by splanchnic resection (Figure 98 page 487) Arrhythmias are not the rule but when they appear they are well shown in the electrocardiogram

Course and prognosis Hypertensive heart disease tends to be a progressive condition leading sometimes rapidly but usually slowly to congestive heart failure in the course of 10 to 20 years The condition begins as a rule in-

sidiously and very gradually in middle life at about forty to fifty years of age and is often discovered in the course of routine blood pressure or cardiac examination (for life insurance for example) When it begins in youth it is more serious when it begins in old age it is not so serious unless coronary disease or cerebral arteriosclerosis complicates the condition Sometimes at first there are merely waves or periods of hypertension with normal pressure between Transient or paroxysmal hypertension may however in the course of time do as much harm to some patients as sustained hypertension in the usual run of cases Even when the hypertension becomes fixed there tend to be waves or periods of considerable increase above the average level for example a systolic pressure of 180 mm may rise to 240 for a few hours at a time on excitement fatigue or from unknown cause There may be a mild and temporary increase of blood pressure or an exacerbation of a pre-existing hypertension at the time of the menopause

The term *malignant hypertension* has been introduced to designate an extreme grade of hypertension with a rapidly fatal course (months to a year or two) Actually however it includes a variety of severe cases those that are marked and serious from the very beginning (usually young adults), those approaching the end of a long hypertensive course and those who after some years of a fairly benign hypertension take a rather abrupt turn for the worse The chief characteristics of malignant hypertension are the high diastolic blood pressure (130 to 140 mm or over) the very abnormal eye grounds and the bad prognosis and rapid course

Although heart failure is the most common of the end results of hypertension cerebral hemorrhage is also frequent angina pectoris and coronary thrombosis are next in order and renal insufficiency is least common In a series of 410 cases of primary or essential hypertension examined post mortem (Bell and Clawson 1928) congestive heart failure was found in 187 cases (44½ per cent) cerebral hemorrhage or thrombosis in 81 cases (19 per cent) coronary heart disease in 67 (16 per cent) renal insufficiency in 36 (8½ per cent) and miscellaneous conditions in 49 (12 per cent) In a later series (1941) of 2 597 hypertensive patients who succumbed to cardiovascular disease Clawson found that death was caused by myocardial insufficiency in 43 3 per cent by coronary heart disease in 36 per cent by cerebral hemorrhage in 13 9 per cent and by renal insufficiency in 6 8 per cent In the series of 375 hypertensive cases studied by Murphy and his associates (1932) heart failure (mostly congestive but including coronary) caused 50 per cent of the deaths, infections 14 2 per cent apoplexy 13 4 per cent and renal failure 10 4 per cent Fahr (1935) put the percentage of deaths in hypertensive cases due to congestive heart failure at 55

Serious prognostic signs are very high diastolic blood pressure (over 130 mm) marked changes in the eye grounds pulsus alternans gallop rhythm and paroxysmal dyspnea or cardiac asthma A serious prognosis should not be given on the finding of slight or moderate hypertension or slight cardiac

enlargement alone Much cardiac enlargement or sustained hypertension of very high degree warrants a grave prognosis

On the other hand within the last decade a change has taken place in the course and probable prognosis of some of the cases of hypertension even of high grade with hypertensive heart disease as the result of the more complete splanchnic sympathectomy carried out by Smithwick (1940 and observations made by myself on his cases 1942–1951) Occasionally striking results have occurred with relief not only of the hypertension eye ground changes and symptoms but also of the physical and electrocardiographic evidences of the heart strain such as gallop rhythm pulsus alternans and *T* wave abnormalities In at least a few of these cases the hypertensive heart disease should be regarded like the thyrotoxic hearts and some instances of acute rheumatism as a reversible process in its acute or subacute stage The strict application of low sodium and of Kempner s rice diets has also reversed or retarded the hypertensive process in some though relatively fewer cases

Complications The most important complications of hypertensive heart disease and their relative frequency have been noted above congestive heart failure apoplexy angina pectoris coronary thrombosis and nephritis with uremia Acute infections are common and may end the story as may also pulmonary embolism from phlebothrombosis in the leg especially after congestive heart failure has set in Arteriosclerosis is almost universally found in older patients with hypertension but although undoubtedly favored by the strain of the high blood pressure it is not by any means a constant finding Types of heart disease other than that due to coronary sclerosis may complicate the enlargement and weakness from hypertension Syphilitic aortitis thyrotoxicosis and rheumatic heart disease are not infrequent complications Hypertension is often found with aortic regurgitation and with mitral disease with or without much stenosis and it is not rare even with aortic stenosis Finally nervousness and neurocirculatory asthenia are common complications of hypertensive heart disease and frequently exaggerate the seriousness of the symptoms and of the condition itself

Treatment The treatment of hypertensive heart disease resolves itself into three parts consisting of (1) the therapy of cardiac complications (2) the therapy of the underlying hypertension and (3) preventive measures to protect the damaged heart

(1) The treatment of the cardiac complications such as congestive failure cardiac asthma angina pectoris coronary thrombosis and atrial fibrillation will be discussed in later chapters of this book mainly in Part IV The presence of hypertension does not in any way contraindicate the usual measures as for example the use of digitalis for failure or for atrial fibrillation of nitrites for angina pectoris of morphine for coronary thrombosis and cardiac asthma and of quinidine for atrial fibrillation It need hardly be added that the most important measure of all not in the emergency but when the emergency is over is an attempt if it seems feasible by medical or surgical measures

(outlined below) even in the absence of specific therapy to reduce the main factor of strain namely the hypertension

(2) The treatment of the hypertension itself continues to be a difficult task in the present state of our knowledge but important studies in progress offer much hope for the future

Drugs Many measures especially medicinal to reduce high blood pressure have been suggested and tried sometimes with slight temporary success sometimes with toxic effects sometimes though rarely with prolonged benefit these include such drugs as the nitrites bismuth subnitrate benzyl benzoate atropine calcium chloride potassium iodide bromides parathyroid preparations theobromine theophylline ethylene diamine (called also aminophylline, and formerly Euphyllin or Metaphyllin), theobromine sodiosalicylate (Diuretin) theobromine sodium acetate (Thesodate) and other diuretics cucurbocitrin (*from watermelon seeds*) papaverine mistletoe (*intrait de gui*) sunflower seeds garlic yohimbine liver extract ovarian extract testosterone chloral hydrate and other sedatives or hypnotics like phenobarbital (Sodium Luminal) cathartics sulphur and the sulphocyanates (thiocyanates) of sodium or potassium In one series of 70 patients with established essential hypertension (Evans and Loughnan 1939) the effects of 33 different preparations and of a placebo on the blood pressure and on the symptoms were observed None produced a satisfactory hypotensive effect Symptomatic improvement greater than that resulting from the placebo followed the use of only six of the drugs namely bismuth subnitrate iodine and iodide bromide Sodium Luminal (phenobarbital) Theominal (theobromine and phenobarbital) and potassium thiocyanate The sedative drugs seemed to have value in temporarily relieving nervous symptoms when these were prominent and since it is now well established that heavy sedation (e g, Sodium Amytal 0 2 gm 3 gr every hour for three doses) frequently reduces hypertensive blood pressure readings markedly even to normal there is an additional good reason therein for the therapeutic use of sedative drugs

There has been in recent years a revival of the use of the thiocyanates (sulphocyanates) and of veratrum viride and various of its derivatives which appear to be more effective in reducing the blood pressure and in relieving symptoms in hypertensive patients than do other drugs However their effect has been often disappointing and sometimes seriously toxic They should be used under close observation best controlled in the case of the thiocyanates by frequent measurements of the concentration of the drug in the blood itself (preferably kept at 6 to 12 mg per 100 cc blood)

Veratrum viride has been in use for many years in the treatment of eclampsia frequently with considerable reduction of blood pressure but complicated by toxic symptoms The drug under various trade names has been in use also for some time in the treatment of essential hypertension with similar results An analysis of its effects has been published by Freis and Stanton (1948) Only recently have satisfactory extracts been made from veratrum in the form of purified alkaloids One of these called protoveratrine from Vera

trum album has given much promise as indicated by its uniform reduction of both systolic and diastolic pressures for several hours at a time without serious toxic symptoms in hypertensive animals and man when given parenterally (Meilman and Krayer 1949) More recently still protoveratrine has been given orally to ambulatory patients with beneficial effects over periods of weeks and months but the dosage has to be very carefully regulated for each individual to obtain the best hypotensive effect with the least toxic result The dosage parenterally varies from 0 25 to 1 0 mg every 6 hours and orally from 0 5 to 2 0 mg every 8 hours This drug has proved to be especially useful in patients who are too old or otherwise unsuitable for lumbodorsal sympathectomy Whether or not protoveratrine or some other even more effective medicament can actually replace operative treatment it is too early to say It should be added that the heart rate as well as the blood pressure is considerably reduced by veratrum derivatives even down to 40 per minute

Other derivatives from veratrum viride that have been used somewhat helpfully in cases of hypertension are Vertavis (15 to 30 Craw units daily) and especially Veriloid which can be given in the dosage of 2 to 3 mg orally every 6 hours (Wilkins Stanton and Freis 1949 Connar Emlet and Grimson 1950) It may be added that atropine should be available to counteract toxic effects from any veratrum preparation

Potassium thiocyanate is conveniently given in the form of a 4 to 8 per cent solution in peppermint water or in a simple syrup such as that of sarsaparilla and in the dosage of one teaspoonful (4 cc) containing 0 16 to 0 32 gm (2½ to 5 gr) three times a day (total of 0 5 to 1 0 gm or 7½ to 15 gr) the dosage varies as circumstances warrant In one of the largest group of cases reported that of 246 by Barker and his associates (1941) symptoms were relieved and blood pressure was reduced in 47 5 per cent in the course of two to four weeks In another series of 50 patients subjective improvement was definite in 63 per cent fair in 20 per cent and disappointing in 17 per cent six showed toxic effects the blood pressure of every patient was somewhat reduced and objective results were considered satisfactory in 78 per cent fair in 16 per cent and poor in 6 per cent the average systolic pressure dropped from 197 mm before treatment to 156 mm with treatment and the average diastolic pressure dropped from 115 to 94 the average maintenance dosage of 5 gr varied from three to twenty-one (average nine) times per week In another group of 20 patients with pronounced arterial hypertension (Blaney Geiger and Ernst 1941) to whom potassium thiocyanate was given after a control period on placebos one half of the total number apparently responded with a complete or partial remission of their hypertension eight of the 16 patients with symptoms felt better during the therapy a few felt worse In still another group 120 hypertensive patients were treated (Caviness and associates 1941) with results recorded as good in 68 9 per cent (reduction of more than 15 per cent in both systolic and diastolic pressures) fair in 11 5 per cent and poor in 19 6 per cent Other authors however have emphasized the toxic effect of the drug (Wald Lindberg and

Barker 1939, Robinson and O Hare 1939), the last named authors reported toxic symptoms in 29 (38 per cent) of their 75 patients less serious in 23 of them (nausea, weakness dermatitis purpura and a decrease in libido) and more serious in the other 6 (dermatitis exfoliativa congestive heart failure cerebral thrombosis angina pectoris and psychoses), but at the same time they believed that there was decided value in the therapy when carefully controlled (maximum drops in blood pressure of over 100 mm systolic and 35 mm diastolic were observed in 3 cases, average drops of 40 mm systolic and 20 mm diastolic in 63 per cent of the patients and relief of hypertensive headaches in 18 out of 20 cases)

Rogers and Palmer (1947) compared the use of thiocyanate therapy in hypertension to sympathectomy by Smithwick s operation, they found that only about one fifth of 100 patients showed any considerable fall in blood pressure from the effect of the drug and that such falls required continuous therapy for their maintenance and were not at all comparable to the drop in pressure obtained in favorable cases by splanchnic resection once in a while however the drug produced brilliant results in the relief of headache

Recent papers on the administration of the thiocyanates emphasize a general dissatisfaction with their use (Ruskin and McKinley 1947) and their greater value in the absence of organic changes (Alstad 1949)

Other drugs more recently introduced with definite hypotensive but generally disappointing effects include tetraethylammonium chloride dihydroergocornine derived from ergot Dibenamine and Driscol Still other medicaments recently recommended but unconfirmed include procaine HCl in honey thyroid extract and Rauwolfia serpentina Rutin a flavone rhamnoglucoside extracted from wheat germ has been used to reduce the hazard of hemorrhage from capillary fragility in essential hypertension but there has been considerable doubt as to its clinical value

Most recently hexamethonium salts have been tried for hypertension (Smirk 1951, Locket et al, 1951 George W Pickering personal communication 1951) it appears to be effective if given intramuscularly 3 or 4 times a day at increasing dosage beginning with 15 mg

Diet Dietary restrictions have been tried particularly the limitation of the total caloric value of the diet of protein food and of common salt Reduction of weight has been carried out with some benefit in a good many obese patients reference has already been made earlier in this chapter (page 468) to the hypotensive effect of starvation with resulting loss of weight.

Two special diets are in common use today in the treatment of hypertension because of their success in some though in the minority of cases One of them introduced years ago emphasized the need of restriction of sodium chloride (Allen 1920) and has been resumed and studied in recent years with variable success It has been shown that it is the sodium content of the diet that is important as it is in the case of the dietary treatment of congestive heart failure in fact it is the hypertensive patient with congestion threatened or present who receives the most benefit Just how on occasion the sodium re

striction acts on hypertension has not yet been elucidated its relationship to adrenal function among other mechanisms has been indicated

The other diet which in recent years has been much utilized in the treatment of hypertension is the rice diet introduced by Kempner (1944) In the first place this diet has about as low a sodium content as it is possible to give (less than 0 5 gm) secondly it is very low also in protein (about 20 gm daily) and thirdly it contains very little fat (about 5 gm daily) It consists of rice fruit and sugar with no other food during the first six weeks or more of treatment but later is liberalized according to circumstances The explanation of its success is still unclear but in those persons who are faithful to it (a minority of cases) there is an improvement of abnormal eye grounds electrocardiogram and heart size and a definite reduction in blood pressure both systolic and diastolic in more than half (the exact percentage has not yet been determined) whether or not there has been a loss of weight There need be no weight loss since the diet contains at least 2 000 calories As in the case of the low sodium diet so here too it is the somewhat congested hypertensive patient who seems to receive the most benefit and also some cases of renal involvement for whom as a matter of fact the diet was first introduced

It should be emphasized that the conscientious following of this rice diet' has been helpful in the case of many hypertensive patients including some not improved by other therapeutic measures medical or surgical including sympathectomy also that it can be added helpfully to other treatment not sufficiently effective per se

Much study remains to be done on the effect of diets on hypertension and it is to be observed also that on occasion there may develop from either of the diets noted above a serious sodium lack requiring emergency treatment

Other medical measures Measures of physical therapy have been advocated rest physical and mental baths of all kinds venesection electrotherapy (high frequency diathermy) and roentgen ray irradiation of the pituitary and adrenal glands Psychotherapy has been used both consciously and unconsciously along with attempt to adjust or to remove strain of professional or business life of family affairs and of social activities Often these measures have been combined in various ways and degrees particularly at special health resorts or spas and often by the family doctor or specialist at home

The imposing list of remedies and their advocacy by so many different persons reveal their very weakness we have not yet a real cure or a specific treatment for hypertension except on the one hand surgical removal of certain unilaterally diseased or deformed kidneys and pheochromocytomata in rare cases and on the other hand thoracolumbar (lumbodorsal) sympathectomy in suitable cases Whether to match the numerous causes of hypertension we may have to develop a variety of cures or whether a single drug or chemical or other measure will neutralize hypertension in the majority of cases no matter what the original cause we do not yet know

Rest either per se or enforced by a stay in a hospital or in bed at home as the result of some illness or surgical operation sometimes materially lowers

a high blood pressure even temporarily to normal if it is not too high to start with but rarely is this effect maintained after the patient has become active again in contrast to the more lasting effect of lumbodorsal splanchnic resection when it is successful as will be recounted below (Rojas et al 1944)

Summarizing the value of the various methods of medical treatment it may be said that a few have been shown to be more useful than others, not as cures but in a palliative way These are (1) a relief from all avoidable nervous and physical strain sometimes in the form of 'rest cures but not an interdiction of moderate healthy outdoor exercise (2) a general reduction of diet not to a weakening starvation level but to one that prevents gain of weight or causes a moderate gradual loss of weight if there is obesity as there so often is in hypertensive cases and especially a reduction of sodium intake as in the rice diet (see above) (3) symptomatic or specific treatment of any particular complicating diseases or disorders including the eradication of such foci of infection as apical tooth abscesses (4) the trial of nerve sedatives and (5) the use of the more successful drugs namely potassium thiocyanate and especially the Veratrum derivatives under careful control as already described Sometimes none of these measures has any effect whatsoever Slight oscillations of blood pressure must not be regarded as important indications of the effect of treatment Relief from all avoidable nervous and physical strain with a healthy regulation of rest, exercise diet and bowel action is of prime importance and sometimes not possible at home where business social and family cares are hard to escape A holiday in some pleasant place or a visit to a good health resort at home or abroad may do much good under such circumstances But whether carried out at home or at a health resort a fall in blood pressure though rarely to normal levels not infrequently follows such therapy

Surgery In late years there have been introduced for the treatment of hyperpiesia certain surgical procedures Decortication of the kidneys has proved ineffective Excision of a deformed or diseased kidney (especially the site of cystic or pyelonephritic degeneration) with the other kidney fairly normal has cured the hypertension in a few cases justifying though to a small degree only the hopes from such a procedure based on the effect of the vascular clamp in experimental animals pleas have been made for conservatism in such surgery so that useful renal tissue may not be sacrificed in vain Extensive bilateral thoracic and lumbar rhizotomy though reported to be effective is too serious and dangerous an operation The value of adrenal denervation and of subtotal adrenalectomy is now being investigated A few spectacular cures have resulted from the exploratory discovery and removal of adrenal tumors (especially the pheochromocytoma responsible for severe paroxysmal hypertension)

Sympathectomy including *splanchnic nerve resection (bilateral)* introduced with the idea of causing a drop in blood pressure as the result of splanchnic and lower limb arteriolar dilatation has been developed to a high degree by a number of surgeons (Peet and associates 1935 1940 1948 Adson and Allen 1940 Smithwick 1940 1948 de Takats and associates 1942

1948 Crutchfield 1947 Poppen 1947 Grimson and Orgain 1948) some of whom most notably Smithwick now denervate both above and below the diaphragm with the result that more and more patients have secured and maintained a distinct hypotensive effect (so great in some cases that at first syncope or near syncope may occur in the erect posture) Smithwick (1940 1942) stated that removal of virtually the entire great splanchnic nerve with division of all of its aortic branches coupled with interruption of the communicating rami of D9 D10 D11 D12 and L1 together with excision of the sympathetic trunk over this area is the minimal procedure found consistently to produce a blood pressure change which is characteristic of a thorough interruption of the nerve supply to the splanchnic bed The younger patients with more labile vasopressor reactions smaller pulse pressures with relatively higher diastolic than systolic levels and less permanent cardiovascular damage have been found most amenable to improvement even though their pressures may be elevated and their fundi seriously affected (and as such belonging to the malignant hypertensive category) Spectacular improvement (perhaps cure) has been noted now in a good many cases but the procedure is still relatively new and has but recently emerged from the experimental stage

Among 224 cases sympathectomized at the Mayo Clinic (Allen and Adson 1940) good results were reported in 13 per cent fair in 18 per cent temporary in 39 per cent and poor in 30 per cent With improved technic consisting for the most part of more extensive sympathectomy better results have been obtained since 1940 Among the larger series of cases treated by experienced surgeons and with better selection than originally the results have been well worthwhile in slightly over half the patients operated upon and followed for several years For example in Smithwick s series of 256 patients with essential including malignant hypertension operated upon by his newer technic between 1938 and 1943 and followed for five to nine years the total mortality was 31 2 per cent distinctly less than the expected rate for similar hypertensive cases not so treated 90 per cent of the survivors were improved symptomatically the eye grounds were improved in 41 per cent the electrocardiograms were better in 42 per cent and the blood pressures were lower in 47 per cent (Smithwick 1948) During the first five year follow up study 84 per cent of the cases had shown a distinct lowering of pressure but a considerable number of these showed a gradual return of blood pressure toward or to the preoperative levels during the later (5 to 9 years) follow up period Palmer (1947) reported a diminishing return of favorable results the longer the patients are followed nearly 70 per cent early in his experience declining to 25 per cent when patients are followed three to five years or more But he writes this effect has been obtained twice as frequently in this series by surgical means as by a careful medical regimen and was obtained in patients with malignant hypertension whose blood pressures were unaffected by medical management Isberg and Peet (1948) have reported that 60 per cent of 384 cases of arterial hypertension were alive 5 to 12 years after splanchnicectomy of the survivors 41 per cent of those with abnormal electrocardiograms showed improvement and 44 per cent of those with

cardiac enlargement showed significant decrease in heart size Another series of 100 consecutive patients were treated by extensive thoracolumbar sympathectomy by the same surgeon and carefully followed for 1½ to 4 years after operation the results were good in 47 per cent fair in 24 per cent and unsatisfactory in 28 per cent, including one operative death and six others who died after discharge from the hospital (Poppen and Lemmon 1947) Grimson and his associates (1949) have reported the results of subtotal to total sympathectomy in 113 patients with severe or moderately severe hypertension followed for one to nine years, 97 of the cases were still living with normal or near normal blood pressure in 31 reduced pressure in 43 more and postural lowering of pressure in all together with improvement in eye grounds in many cases and in electrocardiograms and heart size in a few

I myself have seen many excellent results among the cases sympathectomized by Smithwick not only have the eye grounds cleared and the pressure fallen to normal or near normal but evidences of heavy strain on the heart have also abated including electrocardiographic abnormalities (Figure 97 page 477) (Canabal Thomson and White 1944 White et al 1945) and even on occasion x ray evidence of cardiac enlargement (White 1946 and Figure 98) My own most interesting experience in the treatment of serious hypertensive cardiovascular disease has been summarized in a personal study of 100 cases with important complications including for the most part left ventricular weakness or frank failure but also cerebral vascular lesions angina pectoris and past myocardial infarction Fifty of these cases had thoracolumbar sympathectomy by Smithwick the other cases (controls) of similar sex and age distribution (ratio of 3 men to 1 woman and large majority of cases under the age of 50 in each group) and with similar defects had medical but not specific dietary treatment Each group was followed for a minimum of three years The mortality in a given period of time of the surgical group was less than half that of the medical group and the blood pressures eye grounds electrocardiograms and symptoms were normal or much nearer normal in the majority of the survivors of the surgical group than in the controls The surgical cases who were not helped at all or who were worse or died were further analyzed one patient who had been improved died later of leukemia while 12 of the other 29 cases who died or were not improved could in retrospect have been quickly rejected for sympathectomy by the application of new criteria recently introduced by Smithwick (1950) in which a scoring of adverse points for various abnormalities is made and then the points added up (scores under 4 more suitable for operation than those above) For example an abnormal electrocardiogram is one adverse point x ray evidence of cardiac enlargement another age of 50 years a third and so on Abnormality of renal function is especially serious and in general a contraindication to surgery moderate involvement of the heart however or a cerebral vascular lesion is not a bar per se The borderline group (Smithwick s Group 3) contained 19 of my 50 sympathectomized cases 10 of which turned out well and 9 poorly it is now this group that especially needs further evaluation

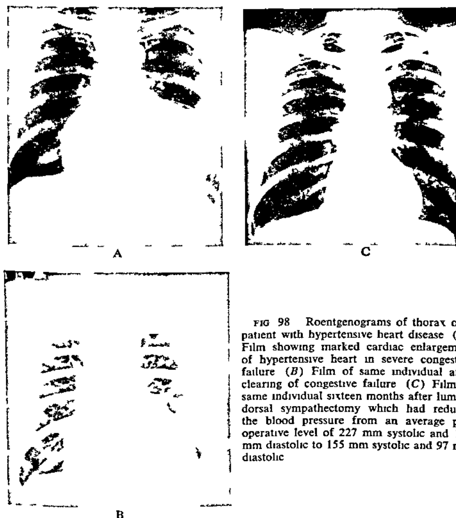
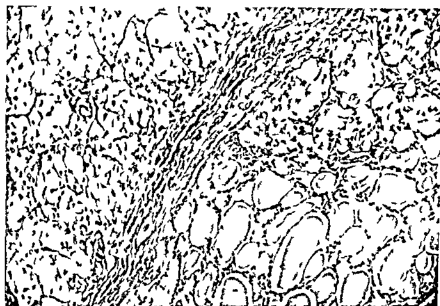


FIG 98 Roentgenograms of thorax of a patient with hypertensive heart disease (*A*) Film showing marked cardiac enlargement of hypertensive heart in severe congestive failure (*B*) Film of same individual after clearing of congestive failure (*C*) Film of same individual sixteen months after lumbo-dorsal sympathectomy which had reduced the blood pressure from an average pre operative level of 227 mm systolic and 120 mm diastolic to 155 mm systolic and 97 mm diastolic

The fact that 5 of my 50 hypertensive cases with grave cardiovascular lesions were perfectly well with normal blood pressure three years or more after operation and that 15 more were distinctly improved is quite clear proof in my experience that hypertensive cardiovascular disease is reversible and that up to the present time sympathectomy has achieved the greatest thera peutic success in this respect

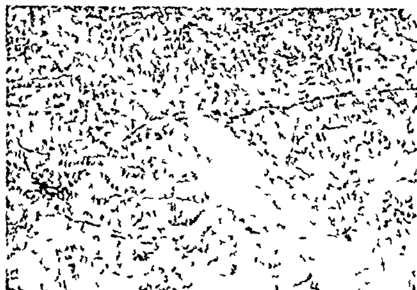
It must be clearly recognized however that this surgical treatment is largely empirical and may be replaced or reinforced later by something better that it is a serious major operative procedure in itself (in fact two operations first on one side and then on the other ten days to two weeks apart) that it is followed by a tedious often uncomfortable convalescence lasting two or three months and that it is not suitable for the majority of patients with hyperten

Fig 67



E *Adenocarcinoma with follicular structure* There is virtually no colloid in the neoplastic acini The tumor extends alongside a septum and invades normal thyroid tissue in the right upper half of this microphotograph Hematoxylin and eosin ×90

Fig 67



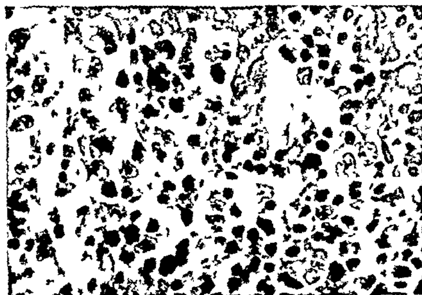
F *Adenocarcinoma* In contrast to Fig E the predominant structure is tubular rather than follicular The epithelial cells are tall columnar and well polarized There is nonetheless a good deal of cellular and structural anaplasia Density and distribution of chromatin vary many nuclei are vacuolated Hematoxylin and eosin ×90

Fig 68



A *Small cell carcinoma* The thyroid gland is completely obliterated by vast numbers of small pleomorphic cells not displaying any pattern There is some resemblance to lymphosarcoma and indeed this type of neoplasm has formerly been so called For details see Fig B Compare with giant cell carcinoma Fig C Hematoxylin and eosin ×90

Fig 6B



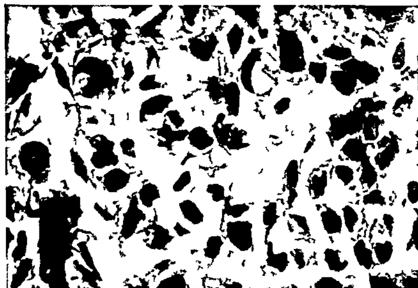
B *Small cell carcinoma high power view* Same slide as Fig A Pleomorphism o shape and size of the cells Many nuclei are pyknotic others contain prominent nucleo, surrounded by loosely arranged chromatin x485

Fig 68



C *Giant cell carcinoma* Solid growth of a very pleomorphic epithelial neoplasm Many nuclei are not only very large but bizarre as well Marked hyperchromatism of nuclei To the left a residual thyroid acinus Hematoxylin and eosin x90

Fig 68



D *Giant cell carcinoma under higher power* Same field as Fig C. Cytoplasm somewhat vacuolated x485

BIBLIOGRAPHY

Part X

1 ZIMMERMAN L M WAGNER D H PERLMUTTER H M and AMROMIN G D Benign and malignant epithelial tumors of the thyroid gland Arch Surg 1950 LX 1183
2 WEGELIN C Handbuch der speziellen pathologischen anatomie und histologie VIII Drusen mit innerer secretion Henke F and Lubarsch O (eds) Berlin Julius Springer 19 6
3 WARREN S Tumors of the thyroid Bulletin N Y Academy of Medicine 1947 XXIII 5
4 FRIEDMAN N B Cellular involution in the thyroid gland Significance of Hurthle cells Jour Clin Endocrinol 1949 IX 874
5 WILLIS R A Pathology of tumours The C V Mosby Co St Louis Mo 1948
6 DOBYNS B M and LENNON B A study of the histopathology and physiologic function of thyroid tumors using radioactive iodine and radioautography Jour Clin Endocrinol 1948 VIII 732
7 LAHEY F H HARE H F and WARREN S Carcinoma of the thyroid Ann Surg 1940 CXII 977
8 CRILE G JR Cancer of the thyroid Jour Clin Endocrinol 1950 X 115
9 GRAHAM ALLEN Malignant epithelial tumors of the thyroid Surg Gynecol and Obstet 1924 XXXIX 781
10 WARREN S Significance of invasion of blood vessels in adenomas of the thyroid gland Arch Path 1931 XI 55
11 COHNHEIM J Einfacher gallertkropf mit metastasen Virchows Arch f path anat u physiol 1876 LXVIII 547
1 WEGELIN C Malignant diseases of the thyroid gland and its relations to goiter in man and animals Cancer Rev 19 8 III 297
13 VON EISELSBERG Über physiologische functionen einer im sternum zur entwicklung gekomennen krebsigen Schilddrusenmetastaste Arch f deutschen pathol Gesellschaft 1894 Bd 48
14 FRAZELL E L and FOOTE F W JR The natural history of thyroid cancer Review of 301 cases Jour Clin Endocrinol 1949 IX 10 3
15 DOBYNS B M and MALOOF F The study and treatment of 119 cases of carcinoma of the thyroid with radioactive iodine Jour Clin Endocrinol 1951 XI 1323
16 BLACK B M Papillary adenocarcinoma of thyroid gland so called lateral aberrant thyroid tumors West Jour Surg Obstet and Gynecol 1948 LVI 134

17 CHESKY V E DRESEL W C and HELLWIG C A Hurthle cell tumors of the thyroid gland a report on 5 cases Jour Clin Endocrinol 1951 xi 1535

18 JAFFE R H Epithelial metaplasia of the thyroid gland with special reference to the histogenesis of squamous cell carcinoma of the thyroid gland Am Jour Path 1937 xiii 671

19 DINSMORE R S DEMPSEY W S and HAZARD J B Lymphosarcoma of the thyroid Jour Clin Endocrinol 1949 ix 1043

20 MAYO C W and SCHLICKE C P Exogenous tumors of the thyroid gland Am Jour Path 1941 xvii 83

21 RICE C O Microscopic metastases in the thyroid gland Am Jour Path 1934 x 407

22 MOORE C E and WALKER W W Metastatic hypernephroma of thyroid gland with subsequent thyroidectomy nephrectomy and resection of pulmonary metastases Surgery 1950 xxvii 9 9

23 COLE W H MAJARAKIS J D and SLAUGHTER D P Incidence of carcinoma of the thyroid in nodular goiter Jour Clin Endocrinol 1949 ix 1007

24 COPE O DOBYNS B M HAMLIN E JR and HOPKIRK J What thyroid nodules are to be feared Jour Clin Endocrinol 1949 ix 101

25 HERMANSON L CARGILL S L and LESSES M F The treatment of nodular goiter Jour Clin Endocrinol and Metab 195 xii 11

26 PEMBERTON J de J and BLACK B M Goiter in children Surgery 1944 xvi 756

27 DUFFY B J JR and FITZGERALD P J Cancer of the thyroid in children report of 8 cases Jour Clin Endocrinol 1950 x 1 96

28 BIELSCHOWSKY F Experimental nodular goiter Brit Jour Exper Path 1945 xxvi 70

29 PURVES H D and GRIESBACH W E Studies on experimental goiter vii Thyroid carcinomata in rats treated with thiourea Brit Jour Exper Path 1946 xxvii 294

30 PURVES H D and GRIESBACH W E Studies on experimental goiter viii Thyroid tumors in rats treated with thiourea Brit Jour Exper Path 1947 xxviii 46

31 MONEY W L and RAWSON R W The experimental production of thyroid tumors in the rat exposed to prolonged treatment with thiouracil Cancer 1950 iii 3-1

32 MORRIS H P DALTON A J and GREEN C D Malignant thyroid tumors occurring in the mouse after prolonged hormonal imbalance during the ingestion of thiouracil Jour Clin Endocrinol 1951 xi 1281

33 GREENE H S N Identification of malignant tissues Jour Am Med Assoc 1948 cxxxvii 1364

34 DOBYNS B M and LENNON B The growth and histologic changes of human thyroidal tumors transplanted into the anterior chamber of the eyes of guinea pigs Jour Clin Endocrinol 1951 xi 1481

35 FITZGERALD P J and FOOTE F W JR The function of various types of thyroid carcinoma as revealed by the radioautographic demonstration of radioactive iodine (I^{131}) Jour Clin Endocrinol 1949 ix 1153

36 MARINELLI L D FOOTE F W HILL R F and HOCKER A F Retention of radioactive iodine in thyroid carcinoma Am Jour Roentgenol and Rad Therapy 1947 lviii 1

37 SEIDLIN S M ROSSMAN I OSHRY E and SIEGEL E Radioiodine therapy of metastases from carcinoma of the thyroid a six year progress report Jour Clin Endocrinol 1949 ix 11

38 RAWSON R W RALL J E and PEACOCK W Limitations and indications in the treatment of cancer of the thyroid with radioactive iodine Jour Clin Endocrinol 1951 xi 11 8

39 RALL J E MILLER W N FOSTER C G PEACOCK W C and RAWSON R W The use of thiouracil in the treatment of metastatic carcinoma of the thyroid with radioiodine Jour Clin Endocrinol 1951 xi 1 73

40 ALBERT A RAWSON R W MERRILL P LENNON B and RIDDELL C B The effect of goitrogenic and other reducing agents on inactivated thyrotropic hormone extract Endocrinology 1947 xl 99

41 LANGE H J and MACLEAN K F Malignant neoplasms of the thyroid Surgery 1949 xvi 86

42 BLACK B M Surgical treatment of carcinoma of the thyroid gland Jour Clin Endocrinol 1949 ix 1422

43 CRILE G JR Treatment of carcinoma of the thyroid with special reference to use of radioactive iodine Cleveland Clinic Quarterly 1952 xix 1

44 CATTELL R B Indications for neck dissection in carcinoma of thyroid Jour Clin Endocrinol 1950 x 1099

45 LAHEY F H and HARE H F Malignancy in adenomas of the thyroid Jour Am Med Assoc 1951 cxlv 689

46 FREEDBERG A S URELES A L LESSES M F and GARGILL S L The successful treatment with radioactive iodine of a solitary pulmonary metastasis from a papillary adenocarcinoma of the thyroid gland apparent cure Jour Am Med Assoc 1950 cxliv 16

47 FREEDBERG A S URELES A L LESSES M F and GARCILI S I Treatment of thyroid carcinoma with radioactive iodine (I^{131}) Am Jour Med 1951 xi 44

48 SZILACYI D L McCLURE R D CONNELL T H WATSON J H L and PREUSS L E Radioiodine (I^{131}) tracer studies after total thyroidectomy Ann Surg 1951 cxxxiv 546

33 GREENE H S N Identification of malignant tissues Jour Am Med Assoc 1948 cxxxvii 1364
34 DOBYNS B M and LENNON B The growth and histologic changes of human thyroidal tumors transplanted into the anterior chamber of the eyes of guinea pigs Jour Clin Endocrinol 1951 xi 1481
35 FITZGERALD P J and FOOTE F W JR The function of various types of thyroid carcinoma as revealed by the radioautographic demonstration of radioactive iodine (I^{131}) Jour Clin Endocrinol 1949 ix 1153
36 MARINELLI L D FOOTE F W HILL R F and HOCKER A F Retention of radioactive iodine in thyroid carcinoma Am Jour Roentgenol and Rad Therapy 1947 lviii 1
37 SEIDLIN S M ROSSMAN I OSHRY E and SIEGEL E Radioiodine therapy of metastases from carcinoma of the thyroid a six year progress report Jour Clin Endocrinol 1949 ix 11
38 RAWSON, R W RALL J E and PEACOCK W Limitations and indications in the treatment of cancer of the thyroid with radioactive iodine Jour Clin Endocrinol 1951 xi 1128
39 RALL J E MILLER W N FOSTER C G PEACOCK W C and RAWSON R W The use of thiouracil in the treatment of metastatic carcinoma of the thyroid with radioiodine Jour Clin Endocrinol 1951 xi 1273
40 ALBERT A RAWSON R W MERRILL P LENNON B and RIDDELL C B The effect of goitrogenic and other reducing agents on inactivated thyrotropic hormone extract Endocrinology 1947 xl 299
41 LANGE H J and MACLEAN K F Malignant neoplasms of the thyroid Surgery 1949 xxi 86
42 BLACK B M Surgical treatment of carcinoma of the thyroid gland Jour Clin Endocrinol 1949 ix 14
43 CRILE G JR Treatment of carcinoma of the thyroid with special reference to use of radioactive iodine Cleveland Clinic Quarterly 1952 xix 1
44 CATTELL R B Indications for neck dissection in carcinoma of thyroid Jour Clin Endocrinol 1950 x 1099
45 LAHEY F H and HARE H F Malignancy in adenomas of the thyroid Jour Am Med Assoc 1951 cxlv 689
46 FREEDBERG A S URELES A L LESSES M F and GARGILL S L The successful treatment with radioactive iodine of a solitary pulmonary metastasis from a papillary adenocarcinoma of the thyroid gland apparent cure Jour Am Med Assoc 1950 cxliv 16

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